Decision Memo for Computed Tomographic Angiography (CAG-00385N)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) has decided to make no change to section 220.1 of the National Coverage Determination Manual titled "Computed Tomography" (Pub. 100-3, 220.1). We have decided that no national coverage determination on the use of cardiac computed tomography angiography for coronary artery disease is appropriate at this time and that coverage should be determined by local contractors through the local coverage determination process or case-by-case adjudication.

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Decision Memo

TO: Administrative File: CAG 00385N
Computer Tomographic Angiography

FROM:

Steve E. Phurrough, MD, MPA
Director, Coverage and Analysis Group

Marcel E. Salive, MD, MPH
Director, Division of Medical and Surgical Services

JoAnna Baldwin, MS
Lead Analyst

Joseph Chin, MD, MS
Medical Officer

SUBJECT: Coverage Decision Memorandum for Cardiac Computed Tomographic Angiography for the Diagnosis of Coronary Artery Disease

DATE: March 12, 2008

I. Decision

The Centers for Medicare and Medicaid Services (CMS) has decided to make no change to section 220.1 of the National Coverage Determination Manual titled "Computed Tomography" (Pub. 100-3, 220.1). We have decided that no national coverage determination on the use of cardiac computed tomography angiography for coronary artery disease is appropriate at this time and that coverage should be determined by local contractors through the local coverage determination process or case-by-case adjudication.

II. Background

Computed tomographic angiography (CTA) is a general phrase used to describe noninvasive imaging of the arteries with various types of computed tomography (CT) machines, such as multislice CT (MSCT), multidetector CT (MDCT), and dual source CT (DSCT).

The use of CTA has increased over the years due to advances in the technology and rapid diffusion of the machines outside the hospital settings. The initial single slice CT machines produced poor quality images. In the late 1990's, 4 slice CT machines were introduced, with 16 slice and 64 slice CT machines following shortly afterwards. Image quality and performance reportedly increased with each model. However, questions remain on the indications for use.

A particular focus has been the use of CTA for evaluation of the coronary arteries in patients with chest pain. Proponents have claimed that cardiac or coronary CTA may reduce the need for invasive coronary angiography for certain patients. Critics have pointed out the lack of evidence on outcomes and the limitations to the technology including uninterpretable/unassessable segments and the health risks from the considerable radiation exposure. Although there are other uses of CTA, this decision focuses only on the use of CTA for the evaluation of the coronary arteries in patients with symptomatic coronary artery disease (e.g., chest pain). Imaging performed on patients without chest pain (asymptomatic patients) would be considered screening and is not an available benefit in the Medicare program.

Chest pain (angina pectoris) can be classified as "typical angina, atypical angina and noncardiac chest pain" (Snow, 2004 – Appendix A). Angina is defined "as a clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arm" (Snow, 2004). Unstable angina is defined as "angina that presents in 1 of 3 principal ways: rest angina, severe new-onset angina, or increasing angina" (Snow, 2004).

Given the prevalence and incidence of CAD in the US, angina has been well studied and evidence-based guidelines are available for unstable and stable angina. The ACC/AHA guidelines on unstable angina (Gibbons, 2007) and chronic stable angina (Gibbons, 2002) are such examples and are well recognized and accepted. Although these guidelines do not directly incorporate coronary CTA, the treatment algorithms provide clues on possible scenarios where CTA may be considered.

For unstable angina, patients who are at high or intermediate short term risk of death (Appendix A) are almost always treated as inpatients in the hospital setting. These patients typically undergo cardiac catheterization and invasive coronary angiography so the role of CTA is very limited (Anderson, 2007). However, "low-risk patients with unstable angina have a short-term risk not substantially different from those with stable angina" and "their evaluation can be accomplished safely and expeditiously in an outpatient setting" (Gibbons, 2002). Risk in patients with unstable angina may be estimated using validated methods such as the TIMI risk score (Antman, 2000) as noted in the ACC/AHA guidelines (Appendix A).

For chronic stable angina, the ACC/AHA and ACP have developed guidelines with treatment algorithms that may also help guide the consideration for use of imaging such as coronary CTA (Gibbons, 2002). Specifically, for patients with chronic stable angina and an intermediate probability of CAD, imaging may be considered when the exercise test does not suggest high risk and there is inadequate information on diagnosis (Appendix A). The guidelines provide a narrow window for the use of imaging. The current recommended approach for risk determination in patients with stable chest pain is based upon the results of exercise testing. The pretest probability of CAD may be determined by several validated methods (Appendix A) such as published models by Diamond and Forrester (1979), Mark (1987) and Pryor (1993).

Appropriateness criteria have also been published (Hendel, 2006). While these were based on consensus, the criteria may provide additional information on specific uses of CTA, especially for those indications which were considered inappropriate. Most studies, as noted in the Blue Cross Blue Shield technology assessments, have not specifically evaluated long term health outcomes but have looked at diagnostic test characteristics and test performance compared to invasive angiography. The question of how coronary CTA may fit into the current recommended clinical pathways needs to be addressed by research and clinical experts.

In addition, there are a number of aspects or dimensions of imaging quality, as noted by Douglas and colleagues (Douglas et al., 2006), that are relevant and applicable to coronary CTA. Many of these aspects are implicit in the process of imaging but being such may be areas that deserve some explicit focus to ensure that quality is maintained and not forgotten in everyday practice.

III. History of Medicare Coverage

Medicare has an NCD, last revised in 1985, that discusses general uses of CT. The policy does not specifically address the use of CTA technology or CT for the diagnosis of CAD as such an indication was not in clinical practice at the time the policy was last updated. Therefore, CTA has never been addressed through national policy and in the absence of national policy that addresses CTA, coverage is at the discretion of local Medicare contractors. The majority of local contractors have similar local coverage determination policies (LCDs) on CTA.

Medicare is a defined benefit program (§ 1812 (Scope of Part A); § 1832 (Scope of Part B) § 1861(s) (Definition of Medical and Other Health Services)). An item or service must fall within a benefit category as a prerequisite to Medicare coverage. CTA may be eligible for coverage under the Social Security Act section 1861(s)(3).

IV. Timeline of Recent Activities

Date	Action
June 13, 2007	CMS opens National Coverage Analysis for CTA.
July 13, 2007	Initial 30-day public comment period ends.
December 13, 2007	CMS posts proposed decision. A second 30-day public comment period begins.
January 12, 2008	The second 30-day public comment period ends.

V. FDA Status

Currently, CT imaging systems and post-processing software go through the 510(k) process at the FDA to obtain clearance for commercial distribution. To obtain 510(k) clearance, the sponsor must demonstrate that the device is substantially equivalent to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). Below are examples of two CT related devices (one CT scanner and one software system) cleared by the FDA through the 510(k) process. The indications for use were copied from the FDA's 510(k) online database at http://www.fda.gov/cdrh/pdf7/K071806.pdf and http://www.fda.gov/cdrh/pdf6/K062386.pdf respectively.

Device Name: ECLOS Computed Tomography X-ray System
Clearance Dated: August 28, 2007
The ECLOS Computed Tomography system is an x-ray imaging device that produces cross-sectional images of the body at different angles. The system reconstructs, processes, displays, and stores the collected images. The device output can provide an aid to diagnosis when used by a qualified physician and is intended for general purpose CT applications.

Device Name: QAngio CT
Clearance Dated: October 5, 2006
QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics. QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists and radiologists.

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix B. In general, features or clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

In this coverage analysis, we considered coronary CTA studies and evidence that were published after the BCBS TEC assessments (published in 2005 and 2006), since the indications are similar. We considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes. Most studies have focused on test characteristics and have not considered health outcomes, such as mortality, morbidity or reduction of invasive angiography. We believe that health outcomes are more important than test characteristics. In evaluating diagnostic tests, Mol and colleagues (2003) reported: “Whether or not patients are better off from undergoing a diagnostic test will depend on how test information is used to guide subsequent decisions on starting, stopping, or modifying treatment. Consequently, the practical value of a diagnostic test can only be assessed by taking into account subsequent health outcomes.” When a proven, well established association or pathway is available, intermediate health outcomes may also be considered. For example, if a particular diagnostic test result can be shown to change patient management and other evidence has demonstrated that those patient management changes improve health outcomes, then those separate sources of evidence may be sufficient to demonstrate positive health outcomes from the diagnostic test.

1. Literature Search

CMS searched PubMed from 2005 to present. General keywords included computed tomographic angiography, CTA and coronary. Initially, we searched for studies that presented original data, examined health outcomes and were published in peer-reviewed English language journals. Since only one study met these criteria, the search was expanded to included technology assessments, meta-analysis, reviews, and studies that reported only test characteristics compared to invasive coronary angiography. Abstracts were excluded.

B. Discussion of evidence reviewed

1. Evidence Questions

a. Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?
b. Is the evidence sufficient to conclude that cardiac CTA reduces the need for invasive coronary angiography?
c. Is the evidence sufficient to conclude that the use of cardiac CTA improves health outcomes for patients with acute chest pain who present in the emergency room or other settings?

2. External technology assessments

DHHS Agency for Healthcare Research and Quality. Non-Invasive Imaging for Coronary Artery Disease. AHRQ 2006; available at: http://www.cms.hhs.gov/determinationprocess/downloads/id34TA.pdf [PDF, 251KB].

In 2006, the Agency for Healthcare Research and Quality commissioned a technology assessment on non-invasive imaging for CAD that was performed by Matchar and colleagues at the Duke Evidence-based Practice Center. For CTA, the authors of the assessment noted: "We identified 29 studies using 16-array or greater multi-detector computed tomography (MDCT) assessing coronary CTA for evaluation of native coronary arteries stenosis, and 13 MRA studies evaluating native coronary artery stenosis using more recent MRI imaging sequences. These studies were generally small, performed at single centers, and often did not include information that would serve to provide confident assessments of the key questions. In particular, we did not identify any studies evaluating the clinical impact of diagnostic strategies including NITs [non-invasive imaging tests] of coronary anatomy compared with strategies that did not include these techniques. The populations studied tended to be relatively young (<65 years of age), and limited results subgrouped by age were available."

They concluded: "At present, there is limited evidence regarding test performance of NITs for identifying, quantifying, or otherwise characterizing coronary artery stenoses. The available evidence provides preliminary data on the ability of coronary MRA (1.5 T) and coronary CTA using at least 16-array MDCT technology to detect obstructive coronary artery lesion in the proximal to mid coronary arteries. The evidence regarding detection of coronary lesions in branch vessels or distal coronary arteries remains unclear and may well improve as the technology improves. Studies conducted to date primarily fall into the "proof of concept" category with study patients having a high pre-test probability of CAD. Patients providing suboptimal images were often excluded from calculations of test accuracy. Future work will need to examine these tests in larger, less selected populations representing the clinical settings in which they are actually expected to be used. The effect of biases in selection of study patients and in the publication of accuracy results for these tests was not assessed in this preliminary analysis."

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 20, No. 4, May 2005.

In 2005, the BCBS TEC published a technology assessment "to evaluate the clinical effectiveness of contrast-enhanced cardiac computed tomographic angiography, hereafter referred to as CTA, for coronary artery evaluation." Study inclusion criteria were (quoted as follows):

- Used contrast-enhanced EBCT with slice thickness no greater than 1.5 mm or contrast- enhanced MDCT with at least 16 rows
- Applied an appropriate reference standard such as conventional coronary angiography or clinical reference standard
- Reported sensitivity and/or specificity of CTA or sufficient data to generate a 2 × 2 contingency table
- Included only human subjects
- Published in English as a full-length, peer-reviewed journal article

Twenty-one studies (16 on MDCT, 6 on EBCT; 1016 total patients) were included in the assessment. The TEC reported:" The evidence is insufficient to determine whether the use of CTA improves net health outcome or whether it is as beneficial as any established alternatives."

The TEC criteria and results were as follows:
1. The technology must have final approval from the appropriate governmental bodies. (Met)
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. (Not met)
3. The technology must improve the net health outcome. (Not met)
4. The technology must be as beneficial as any established alternatives. (Not met)
5. The improvement must be attainable outside the investigational settings. (Not met)
They concluded that: "the use of contrast-enhanced cardiac CT angiography for screening or diagnostic evaluation of the coronary arteries does not meet the TEC criteria."

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 21, No. 5, August 2006.

In 2006, the BCBS TEC published an update of their 2005 assessment of CTA. The objective was "to determine the usefulness of CTA as a substitute for coronary angiography for two indications: 1) in the diagnosis of coronary artery stenosis, and 2) in the evaluation of acute chest pain in the emergency room (ER)." The TEC report focused on "studies examining 64-row CTA, which provides better resolution than the previous generation of 16-row machines." For CTA as a substitute for invasive angiography, study inclusion criteria were (quoted as follows):

- Used contrast-enhanced EBCT with slice thickness no greater than 1.5 mm or contrast- enhanced MDCT with at least 32 rows
- Applied the reference standard of invasive angiography to all patients
- Reported sensitivity and/or specificity of CTA or sufficient data to generate a 2×2 contingency table
- Included only human subjects
- Published in English as a full-length, peer-reviewed journal article

For CTA in the ER; "prospective studies were selected in which patients meeting specific chest pain and clinical criteria for evaluation with CTA were chosen to have the test."

Seven studies (480 patients) were evaluated for CT diagnostic accuracy, and 2 studies (100 patients) for CTA in the ER. The TEC reported: "The available evidence is inadequate to determine whether CTA improves the net health outcome or is as beneficial as established alternatives for diagnosis of coronary artery stenosis or for evaluation of acute chest pain in the ER."
The TEC criteria and results were as follows:
1. The technology must have final approval from the appropriate governmental bodies. (Met)
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. (Not met)
3. The technology must improve the net health outcome. (Not met)
4. The technology must be as beneficial as any established alternatives. (Not met)
5. The improvement must be attainable outside the investigational settings. (Not met)
They concluded: "CTA as a substitute for coronary angiography in the diagnosis of coronary artery stenosis does not meet the TEC criteria. CTA in the evaluation of acute chest pain in the emergency room also does not meet the TEC criteria."

3. Internal technology assessments

Meta-Analyses

Hamon M, Biondi-Zoccai G, Malagutti P, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography. A meta-analysis. J Am Coll Cardiol 2006;48:1896 –1910.

In 2006, Hamon and colleagues reported the results of a meta-analysis "to define the current role of multislice spiral computed tomography (MSCT) for the diagnosis of coronary artery disease (CAD) using a meta-analytic process." The authors included 29 studies (2024 patients), published from 2002 to 2006, that evaluated the coronary arteries using both CTA (at least 16 slice) and conventional coronary angiography. Study inclusion criteria were: "1) it used MSCT as a diagnostic test for obstructive CAD, with >50% diameter stenosis selected as the cut-off criterion for significant CAD, using conventional invasive angiography as the reference standard; 2) it used the newest generation of MSCT ($\geq$16 slices); and 3) it reported cases in absolute numbers of true positive (TP), false positive (FP), true negative (TN), and false negative (FN) results or presented sufficiently detailed data for deriving these figures." Exclusion criteria were studies performed: "1) only in patients after coronary artery bypass graft surgery; 2) after percutaneous coronary intervention for long-term stent patency assessment; 3) in a subset of patients with prior heart transplant; or 4) with fewer than 30 enrolled patients." Patient symptomatology was not specified. A random-effects model was used for the analysis.

The authors noted a considerable percentage of uninterpretable segments that were excluded from the analysis by the study investigators. Pooled sensitivity, specificity, positive and negative predictive values per-segment were 81%, 93%, 67.8% and 96.5%, respectively, and per patient were 96%, 74%, 83% and 94%, respectively.

The authors concluded: "Multislice spiral computed tomography has shortcomings difficult to overcome in daily practice and, at the more clinically relevant per-patient analysis, continues to have moderate specificity in patients with high prevalence of CAD. Studies evaluating the diagnostic performance of the newest generation of MSCT, including patients with low to moderate CAD prevalence, will be critical in establishing the clinical role of this emerging technology as an alternative to CA."

Schuijf JD, Bax JJ, Shaw LJ, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. Am Heart J 2006;151:404-11.

In 2006, Schuijf and colleagues reported the results of a meta-analysis "to clarify the current accuracy of both modalities in the detection of significant coronary artery lesions (compared to conventional angiography as the gold standard)." The authors included 24 studies (1300 patients), published from 2001 to 2005, that compared MSCT (4 to 16 slice) to invasive coronary angiography in patients with known or suspected CAD. Reports with insufficient data to calculate sensitivity and specificity were excluded. Meta-analysis model was not specified. Summary odds ratios were calculated using the "Comprehensive Meta Analysis" program. The authors reported pooled test parameters as follows: sensitivity 85%, specificity 95%, PPV 76% and NPV 97%. They concluded: "Meta-analysis of the available studies with MRI and MSCT for noninvasive coronary angiography indicates that MSCT has currently a significantly higher accuracy to detect or exclude significant coronary artery disease."

Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: A meta-analysis. European Journal of Radiology 2006;60:279–286.

In 2006, Sun and Jiang reported the results of a meta-analysis to determine "the diagnostic value of multislice CT (MSCT) angiography in the detection of coronary artery disease (CAD) when compared to conventional coronary angiography." The authors included 47 studies (3149 patients), published from 2001 to 2006, that studied at least 4 slice CT. Study inclusion criteria were: "(a) patients undergoing both MSCT angiography and coronary angiography examinations; (b) studies included at least 10 patients; (c) assessment or comparison of MSCT angiography with coronary angiography was focused on the visualization of coronary arteries and detection or exclusion of coronary artery stenosis; (d) diagnostic value of MSCT angiography was addressed when compared to coronary angiography in terms of sensitivity, specificity, either segments-, vessels- or patients-based assessment." Exclusion criteria, study types, patient symptomatology and setting were not specified. Model for analysis was not specified.

The authors reported pooled sensitivities and specificities for 4, 16 and 64 slice CT in the detection of CAD (76%, 93%; 82%, 95%; 92%, 94%; respectively). They concluded that: "MSCT angiography has potential diagnostic accuracy in the detection of CAD. Diagnostic performance of MSCT angiography has been significantly improved with the latest 64-slice CT, with resultant high qualitative and quantitative diagnostic accuracy. 16-slice CT was limited in spatial resolution which makes it difficult to perform quantitative assessment of coronary artery stenoses."

Systematic Reviews

Janne d'Othee B, Siebert U, Cury R, et al. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. European Journal of Radiology 2007, in Press.

In 2007, Janne d'Othee and colleagues reported the results of a systematic review to estimate sensitivity and specificity of various imaging modalities. Studies were included if they "used contrast-enhanced CT as a diagnostic test, evaluated native coronary arteries, used catheter-based coronary angiography (CCA) as a reference standard independently of CT findings, reported raw data (i.e., numbers that allowed recalculation of 2×2 contingency tables), and were published in peer reviewed journals." Coronary artery bypass graft and coronary stent studies were excluded. Catheter based coronary angiography was the reference standard.

Forty-one studies (2515 patients) were analyzed. A random effects model was used to calculate summary estimates. The authors reported: "Analysis of all coronary segments yielded a sensitivity of 95% (80%, 89%, 86%, 98% for electron beam CT, 4/8-slice, 16-slice and 64-slice MDCT, respectively) for a specificity of 85% (77%, 84%, 95%, 91%)." They noted: "In conclusion, recent advances in CT technology have resulted in an increase in the proportion of coronary segments assessable by CT and in improved diagnostic accuracy from EBCT to 4/8, 16, and 64-slice MDCT. The latter improvement is best demonstrated by the all-segment analysis. With current 64 slice scanners, diagnostic accuracy of CE-CCT is high on a per segment basis. Per patient however, this accuracy may be lower in patients with multi-vessel disease, which may limit the clinical utility of CT in populations at high risk for CAD. The utility of CT in patients with intermediate risk for CAD remains to be established."

Stein PD, Beemath A, Kayali F, et al. Multidetector computed tomography for the diagnosis of coronary artery disease: a systematic review. American Journal of Medicine 2006;119: 203-216.

In 2006, Stein and colleagues reported the results of a meta-analysis "to determine the sensitivity and specificity of contrast-enhanced multidetector computed tomography (CT) for the detection of coronary artery disease." The authors included 33 studies (1606 patients), published from 2001 to 2005, that compared MSCT (4 to 16 slice and 1 study on 64 slice) with invasive coronary angiography. Studies were included if they reported type of machines, data on sensitivity and specificity and patient selection criteria. Abstracts, in vitro studies, series with $\leq$ 10 patients were among those excluded. Meta-analysis model was not specified. Average sensitivity and specificity were calculated from pooled data.

The authors reported: "Average sensitivity for patient-based detection of significant (>50% or $\geq$50%) stenosis was 61 of 64 (95%) with 4-slice CT, 276 of 292 (95%) with 16-slice CT, and 47 of 47 (100%) with 64-slice CT. Average specificity was 84% for 4-slice CT, 84% for 16-slice CT, and 100% for 64-slice CT." They concluded: "Multidetector CT has the potential to be used as a screening test in appropriate patients. Contrast-enhanced 16-slice CT seems to be reasonably sensitive and specific for the detection of significant coronary artery disease but has shortcomings. Preliminary data with 64-slice CT suggest that it is more sensitive and specific."

16 Slice MSCT

Garcia MJ, Lessick J, Hoffmann MHK, CATSCAN investigators. Accuracy of 16-Row Multidetector Computed Tomography for the Assessment of Coronary Artery Stenosis. JAMA 2006;296:403-411.

In 2006, Garcia and colleagues reported the results of a case series of 238 patients "to determine the diagnostic accuracy of 16-row MDCT for the detection of obstructive coronary disease." Included patients were between 30 and 70 years of age who were referred for clinically indicated nonemergency coronary angiography, for evaluation of chest pain, and for intermediate or high probability of disease. Exclusion criteria included prior bypass surgery, arrhythmias, pacemakers/defibrillators, renal insufficiency and contrast allergy. MDCT was performed using 16 row scanners and was done prior to invasive angiography. Invasive angiography was the reference standard. Of the 238 patients, 187 underwent 16 row MDCT with contrast and β blocker drugs. Forty-five percent of patients were classified as intermediate probability for CAD and 55% as high probability, according to the ACC/AHA guidelines (Gibbons et al., 2002). Invasive angiography was the reference standard. Mean age was 60 years. Men comprised 68% of the study population. Of the 1629 segments, 29% were uninterpretable.

The authors reported: After censoring all nonevaluable segments as positive, the sensitivity for detecting more than 50% luminal stenoses was 89%; specificity, 65%; positive predictive value, 13%; and negative predictive value, 99%. In a patient-based analysis, the sensitivity for detecting patients with at least 1 positive segment was 98%; specificity, 54%; positive predictive value, 50%; and negative predictive value, 99%."

The authors concluded: "The results of this study indicate that MDCT coronary angiography performed with 16-row scanners is limited by a high number of nonevaluable cases and a high false-positive rate. Thus, its routine implementation in clinical practice is not justified. Nevertheless, given its high sensitivity and negative predictive value, 16-row MDCT may be useful in excluding coronary disease in selected patients in whom a false-positive or inconclusive stress test result is suspected." There was no follow-up on health outcomes.

Hoffmann MHK, Shi H, Schmitz BL, et al. Noninvasive coronary angiography with multislice computed tomography. JAMA 2005;293:2471-2478.

In 2005, Hoffmann and colleagues reported the results of a case series of 103 patients "to assess the accuracy and robustness of MSCT vs the criterion standard of invasive coronary angiography for detection of obstructive coronary artery disease." All patients had suspected CAD, were in sinus rhythm, were able to hold their breath for 25 seconds, and had been referred for invasive coronary angiography prior to inclusion in the study. Exclusion criteria included prior revascularization, renal insufficiency and contrast allergy. Scans were performed using a 16 detector MSCT with contrast and β blocker drugs. Pretest probability for CAD was assessed according to ACC/AHA guidelines (Gibbons et al., 2002). Invasive coronary angiography was the reference standard. Mean age was 62 years. Men comprised 69% of the study population. For CAD, 2% were determined to have low probability; 63% at intermediate probability; and d 35% at high probability.

The authors reported: "Compared with invasive coronary angiography for detection of significant lesions (>50% stenosis), segment-based sensitivity, specificity, and positive and negative predictive values of MSCT were 95%, 98%, 87%, and 99%, respectively." These estimates excluded 27% of the study patients who had "only partial coronary tree coverage available." Of the 1384 segments, 88 (6.4%) were uninterpretable. Sensitivity, specificity, and positive and negative predictive values per patient were 97%, 87%, 90%, 95%, respectively. The authors concluded: "Multislice computed tomography provides high accuracy for noninvasive detection of suspected obstructive coronary artery disease. This promising technology has potential to complement diagnostic invasive coronary angiography in routine clinical care." There was no follow-up on health outcomes.

Kuettner A, Beck T, Drosch T, et al. Diagnostic accuracy of noninvasive coronary imaging using 16-detector slice spiral computed tomography with 188 ms temporal resolution. J Am Coll Cardiol 2005;45:123–127.

In 2005, Kuettner and colleagues reported the results of a case series of 72 patients "to evaluate the diagnostic accuracy of 16-multi-detector spiral computed tomography (MDCT) with 188 ms temporal resolution." All patients were scheduled for invasive angiography and also underwent MDCT imaging. Exclusion criteria include arrhythmias, renal insufficiency and contrast allergy. Scans were performed using 16 detector MDCT with contrast and β blocker drugs. Pretest probability was not specified. Invasive angiography was the reference standard. Mean age was 64 years. Men comprised 63% of the study population.

The authors reported: "Sensitivity, specificity, and positive and negative predictive values for the whole study group were as follows: 82%, 98%, 87%, and 97%, respectively. The correct clinical diagnosis of presence or absence of significant CAD was obtained in 65 of 72 (90%) patients." Of the 936 segments, 62 (6.6%) were uninterpretable. Per patient estimates were not reported. The authors noted: "In conclusion, noninvasive MDCT imaging is becoming more and more accurate. However, further improvements of spatial and temporal resolution are still required to challenge diagnostic invasive coronary angiography." There was no follow-up on health outcomes.

Mollet NR, Cademartiri1 F, Mieghem CV, et al. Adjunctive value of CT coronary angiography in the diagnostic work-up of patients with typical angina pectoris. European Heart Journal 2007;28:1872–1878.

In 2007, Mollet and colleagues reported the results of a consecutive series of 62 patients "to determine the adjunctive value of CT coronary angiography (CTCA) in the diagnostic work-up of patients with typical angina pectoris." Patients included had typical angina, sinus heart rhythm and were able to hold their breaths for at least 20 seconds. Exclusion criteria included arrhythmias, renal insufficiency and contrast allergy. Scans were performed using 16 slice CT with contrast and β blocker drugs. Pre-test probability was high (81%). Invasive angiography was the reference standard. Mean age was 59 years. Men comprised 73% of the study population.

The authors reported sensitivity, specificity, PPV, NPV of 100%, 87%, 96%, 100%, respectively, per patient. They concluded: "Non-invasive CTCA is a potentially useful tool, in the diagnostic work-up of patients with typical angina pectoris, both to detect and to exclude significant CAD." They also noted: "We have studied a relatively small number of patients who are at high risk of having significant CAD and excluded a significant number of patients because of logistic inability to perform CTCA before the conventional angiogram." Health outcomes were not reported.

64 Slice MSCT

Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-slice computed tomography coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007 (online);doi:10.1136/hrt.2006.112771.

In 2007, Meijboom and colleagues reported the results of a non-consecutive case series of 104 patients to study "the diagnostic performance of 64-slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome." Patients presented with either unstable angina or non-ST elevation myocardial infarction. Exclusion criteria included atrial fibrillation, renal insufficiency and contrast allergy. Scans were performed using 64 slice CT with contrast and β blocker drugs. Pre-test probability was either high (68%) or low with positive or inconclusive exercise tests or high suspicion of CAD (32%). Invasive angiography was the reference standard. Mean age was about 59 years. Men comprised 72% of the study population.

The authors reported sensitivity, specificity, PPV, NPV of 100%, 75%%, 96%, 100%, respectively, per patient. Of the 1525 segments evaluated, 243 (15.9%) were not visualized and excluded. They concluded: "64-slice CT angiography has a high sensitivity to detect significant coronary stenoses and is reliable to exclude the presence of significant coronary artery disease in patients who present with a non-ST elevation acute coronary syndrome. The role of CT coronary angiography in these patients, particular in the lower risk group, needs to be further evaluated." Health outcomes were not reported.

Francone M, Napoli A, Carbone I, et al. Noninvasive imaging of the coronary arteries using a 64-row multidetector CT scanner: initial clinical experience and radiation dose concerns. Radiol med 2007;112:31–46.

In 2007, Francone and colleagues reported the results of a case series of 114 patients to evaluate 64 detector CT. Of the 114 patients, 23 patients had MDCT to evaluate the coronary arteries for typical or atypical chest pain, 37 for evaluation of stent patency, 40 for patency of bypass grafts, 3 for inconclusive myocardial perfusion scintigraphy, and 11 for inconclusive stress echocardiography. Exclusion criteria included arrhythmia, kidney failure and contrast allergy. Scans were performed using 64 detector MDCT with contrast and β blocker drugs. Pretest probability was not reported. No reference standard was specified. Mean age was 63 years. Findings were not separately presented for the group of patients with chest pain. Test parameters and assessable segments were not reported.

The authors concluded: "In our initial clinical experience, the use of 64-MDCT has provided very promising results. Although the technique needs to be validated with systematic comparisons with clinical, laboratory and coronarographic data, the latest generation of 64-MDCT scanners offers new possibilities for clinical management of patients with coronary artery disease. The increase in spatial and temporal resolution translates into improved diagnostic image quality with respect to previous generations of multidetector devices. Thus, 64-MDCT is a noninvasive technique capable of identifying patients requiring interventional or surgical procedures such as selective coronarography with primary angioplasty or stent placement, or surgical revascularisation with bypass grafts. The use of suitable systems for the automatic control of radiation exposure seems nonetheless indispensable in order to limit patient dose, which given the current state of affairs is the main limitation to the clinical use of the technique."

Ehara M, Surmely J, Kawai M, et al. Diagnostic accuracy of 64-slice computed tomography for detecting angiographically significant coronary artery stenosis in an unselected consecutive patient population. Circ J 2006;70:564–571.

In 2006, Ehara and colleagues reported the results of a case series of 69 patients "to investigate the accuracy of 64-slice MSCT (64 MSCT) in daily practice, without any patient selection." Nineteen patients with suspected CAD, 50 patients with proven CAD were enrolled. Exclusion criteria included arrhythmias, renal insufficiency and contrast allergy. Scans were performed using a 64 slice MSCT machine with contrast and β blocker drugs as needed. Pretest probability was not specified. Reference standard was invasive angiography. Mean age was 67 years. Men comprised 75% of the study population.

The authors reported: "Compared with ICAG (invasive coronary angiography) the sensitivity of CTA to diagnose significant stenosis was 90%, specificity 94%, positive predictive value (PPV) 89% and negative predictive value (NPV) 95%. With regard to 58 stented lesions, the sensitivity, specificity, PPV and NPV were 93%, 96%, 87% and 98%, respectively. On the patient-based analysis, the sensitivity, specificity, PPV and NPV of CTA to detect CAD were 98%, 86%, 98% and 86%, respectively." Of the 966 segments, 82 (8%) were uninterpretable. The authors concluded: "Sixty-four-MSCT has a high accuracy for the detection of significant CAD in an unselected patient population and therefore can be considered as a valuable noninvasive technique." No health outcomes were reported.

Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64- X 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343–348.

In 2006, Ropers and colleagues reported the results of a case series of 84 patients to analyze "the accuracy of 64 -slice MDCT coronary angiography for the detection of significant coronary artery stenoses compared with quantitative coronary angiography." All patients enrolled in the study had been referred for invasive angiography due to suspected CAD. Exclusion criteria included acute coronary syndromes, arrhythmias, and contrast allergy. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Pretest probability was not specified. Invasive angiography was the reference standard. Mean age was 58 years. Men comprised 62% of the study population. The authors reported: "After exclusion of unevaluable coronary segments (4%), multidetector computed tomography demonstrated a sensitivity of 93%, a specificity of 97%, and a negative predictive value of 100% in a per-segment analysis. In a per-artery analysis, 15 of 336 arteries (4%) were unevaluable. Sensitivity and specificity in evaluable arteries were 95% and 93%, respectively. In a per-patient analysis (81 of 84 patients included), sensitivity and specificity were 96% and 91%, respectively."

Other Nonspecified CTA

Budoff MJ, Gopal A, Gul KM, et al. Prevalence of obstructive coronary artery disease in an outpatient cardiac CT angiography environment. International Journal of Cardiology 2007; In Press.

In 2007, Budoff and colleagues reported the results of a descriptive study of 493 patients "to determine the prevalence of significant obstructive disease and non-diagnostic studies using coronary computed tomographic angiography (CTA) in an outpatient environment, to establish if CTA could help avoid unnecessary diagnostic cardiac catheterizations." All patients that received CTA "over one year with an indication that could warrant a cardiac catheterization to establish the presence or absence of coronary artery disease (CAD)." Exclusion criteria included prior myocardial infarction, revascularization and congenital heart diseases. "Referred patients generally had an intermediate pre-test probability of obstructive disease (20–80%)." Specific pretest probabilities were not noted. Scans were performed using an electron beam scanner with unspecified detectors. Reference standard was not used for all patients. Mean age was 58 years. Men comprised 68% of the population. The authors reported: "Of the 493 index cases evaluated, 157 (32%) cases were reported to be normal, 204 patients were classified as having nonobstructive disease (41%), 93 patients were defined to have obstructive CAD (19%), and 39 cases were inconclusive (8%)." Sensitivity, specificity and predictive values were not reported. In this study, there was no comparison test. There was no follow-up on health outcomes and patients who received invasive angiography subsequently.

Dual Source CT

Heuschmid M, Burgstahler C, Reimann A, et al. Usefulness of noninvasive cardiac imaging using dual-source computed tomography in an unselected population with high prevalence of coronary artery disease. Am J Cardiol 2007;100:587–592.

In 2007, Heuschmid and colleagues reported the results of a case series of 51 patients "to evaluate the diagnostic accuracy of new DSCT in unselected patients with a high prevalence of CAD, irregular heart rate, and extensive calcific deposits." All patients were scheduled for invasive angiography due to CAD. Exclusion criteria were unstable angina, renal insufficiency, allergy to contrast. Scans were performed using DSCT with contrast. Pretest probability was not specified. Invasive angiography was the reference standard. Mean age was 64 years. Men comprised 73% of the study population.

The authors reported: Based on a coronary segment model, sensitivity was 96%, specificity 87%, positive predictive value 61%, and negative predictive value 99% for the detection of significant lesions (>50% diameter stenosis)." Of the 632 segments that were not stented, 117 (18.5%) were uninterpretable. They concluded: "our initial data indicate that DSCT allows a high accuracy to exclude relevant coronary stenosis in unselected patients with a high prevalence of CAD and a relevant number with heart rhythm irregularities. However, overestimation of stenosis, especially in cases of calcifications, is still a limitation." There was no follow-up on health outcomes.

Weustink AC, Meijboom WB, Moller NR, et al. Reliable high-speed coronary computed tomography in symptomatic patients. J Am Coll Cardiol 2007;50:786–794.

In 2007, Weustink and colleagues reported the results of a case series of 100 patients with chest pain "to prospectively evaluate the diagnostic performance of the high-speed dual-source computed tomography scanner (DSCT), with an increased temporal resolution (83 ms), for the detection of significant coronary lesions ($\geq$50% lumen diameter reduction) in a clinically wide range of patients." All patients were symptomatic with "atypical angina, typical angina, and unstable coronary artery disease (unstable angina or non–ST segment elevation myocardial infarction) scheduled for conventional coronary angiography (CCA)." Patients with arrhythmias, past percutaneous coronary intervention, or bypass surgery, and allergy to contrast were excluded. Scans were performed using DSCT with contrast with nitroglycerin medication. Pretest probability was not specified. Invasive angiography was the reference standard. Mean age was 61 years. Men comprised 79% of the study population.

The authors reported: "Sensitivity, specificity, and positive and negative predictive values of DSCT coronary angiography for the detection of significant lesions on a segment-by-segment analysis were 95% (95% confidence interval [CI] 90 to 97), 95% (95% CI 93 to 96), 75% (95% CI 69 to 80), 99% (95% CI 98 to 99), respectively, and on a patient-based analysis 99% (95% CI 92 to 100), 87% (95% CI 65 to 97), 96% (95% CI 89 to 99), and 95% (95% CI 74 to 100), respectively." Image quality was poor in 14% of the coronary segments. They concluded: "Dual source computed tomography scanner coronary angiography demonstrated a high diagnostic accuracy for the detection or exclusion of significant stenoses in patients with various heart rates without exclusion of unevaluable segments. These results indicate that the technique may now be tested in a cohort with a low-to-intermediate pretest probability of coronary artery disease or in patients with nonanginal chest pain to establish the role of DSCT coronary angiography in the management of patients with suspected coronary artery disease."

Scheffel H, Alkadhi H, Plass A, et al. Accuracy of dual-source CT coronary angiography: first experience in a high pre-test probability population without heart rate control. Eur Radiol 2006;16:2739–2747.

In 2006, Scheffel and colleagues reported the results of a case series of 30 patients "to assess the diagnostic accuracy of dual source computed tomography (DSCT) for evaluation of coronary artery disease (CAD) in a population with extensive coronary calcifications without heart rate control." Thirty patients who had invasive coronary angiography were included in the study. DSCT was performed within 30 days of catheterization. Exclusion criteria included previous stent or bypass surgery, renal insufficiency and contrast allergy. Scans were performed using DSCT with contrast and nitrate drugs. Based on a clinical score developed by Morise and colleagues (Morise et al., 1997), all patients were determined to have high pre-test probability of CAD. Invasive coronary angiography was the reference standard. Mean age was 63 years. Men comprised 80% of the study population.

The authors reported: "Overall sensitivity, specificity, positive and negative predictive value for evaluating CAD were 96.4, 97.5, 85.7, and 99.4%, respectively." Of the 420 coronary segments, 6 (1.4%) were uninterpretable. They concluded: "First experience indicates that DSCT coronary angiography provides high diagnostic accuracy for assessment of CAD in a high pre-test probability population with extensive coronary calcifications and without heart rate control. Further studies are needed to confirm our results in appropriate clinical settings with larger patient populations."

CTA of the coronary arteries in the ER Compared to Invasive Coronary Angiography

Goldstein JA, Gallagher MJ, O'Neil WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863–871.

In 2007, Goldstein and colleagues reported the results of a randomized controlled trial "to compare the safety, diagnostic efficacy, and efficiency of multi-slice computed tomography (MSCT) with standard diagnostic evaluation of low-risk acute chest pain patients." Inclusion criteria were chest pain or angina equivalent symptoms compatible with ischemia during the past 12 hours, age $\geq$25 years; and a prediction of a low risk of infarction and/or complications. Estimation of risk was done using a previously published clinical decision rule (Reilly et al., 2002). Exclusion criteria included known coronary artery disease, electrocardiograms diagnostic of cardiac ischemia and/or infarction, elevated serum biomarkers, contraindication to iodinated contrast and/or beta -blocking drugs, and atrial fibrillation or markedly irregular rhythm. Outcomes included safety, diagnostic efficacy, time and cost of care. Of the 197 patients, 99 were randomly assigned to receive MSCT (64 slice) with contrast and β blocker drugs and 98 to standard care (nuclear stress testing). Mean age was about 50 years. Men comprised about 50% of the study population. Almost all patients (196/197) were determined to be at very low risk using the Goldman Reilly criteria.

The authors reported no deaths, no myocardial infarctions, or other major adverse events in either group at 6 months. There was a significant difference in the proportion of patients discharged home from the ER (88% in the MSCT group versus 97% in the SOC group; p-value=0.03). The number of cardiac catheterizations at 6 months were not significantly different (12% in the MSCT group versus 7% in the SOC group; p-value=0.24). The MSCT scans were considered inadequate in 24.1% (24/99) of the patients and these patients then underwent nuclear stress testing. The authors concluded: "Multi-slice computed tomographic coronary angiography can definitively establish or exclude coronary disease as the cause of chest pain. However, inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations."

Olivetti L, Mazza G, Volpi D, et al. Multislice CT in emergency room management of patients with chest pain and medium-low probability of acute coronary syndrome. Radiol med 2006);111:1054–1063.

In 2006, Olivetti and colleagues reported the results of a case series of 31 patients "to evaluate the diagnostic accuracy of a 16-channel computed tomography (CT) scanner with dedicated software in a group of patients with chest pain and medium to low risk of ACS." Inclusion criteria was "chest pain that was defined as medium to low probability of ACS" (absence of ischemic ECG ST changes and negative serum biomarkers). Exclusion criteria included previous revascularization, elevated heart rate, arrhythmias, various cardiac devices, and adverse reactions to contrast material. Scans were performed using 16 channel MDCT with contrast and β blocker drugs. Invasive angiography was the reference standard. Mean age was 59 years. Men comprised 61% of the study population. All patients received CT imaging and coronary angiography. The authors reported: "sensitivity of 65%, a specificity of 98.8%, a positive predictive value (PPV) of 81.2%, a negative predictive value (NPV) of 97.3% and an accuracy of 96.4%." Of the 469 segments visualized, 383 (81.7%) were considered assessable. Image quality was considered "poor" in 19.8% of the segments (76/383). The authors concluded: "Due to its high NPV, this technique can rule out significant stenoses or coronary occlusions provided that image quality is excellent. In patients with a medium to low coronary risk, MSCT is a more accurate indicator of the need for coronary angiography than is exercise stress testing, which is less expensive but has lower predictive values."

Since our proposed decision, the following additional articles were reviewed.

Brodoefel H, Reimanna A, Burgstahler C, et al. Noninvasive coronary angiography using 64-slice spiral computed tomography in an unselected patient collective: Effect of heart rate, heart rate variability and coronary calcifications on image quality and diagnostic accuracy. European JournalofRadiology2007:http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T6F-4P2JD05-1&_user=10843&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000000150&_version=1&_urlVersion=0&_userid=10843&md5=19427c64306e164f0d1e2fb4392e5971 (in press).

Brodoefel and colleagues reported the results of a case series of 102 patients "to assess the effect of higher heart rates on diagnostic accuracy of 64-slice coronary angiography." All patients were "scheduled for conventional coronary angiography (ICA) due to suspected coronary artery disease (CAD) or suspected progression of known CAD." Exclusion criteria included prior revascularization, chronic congestive heart failure (NYHA III–IV), renal insufficiency and allergy to contrast media. Scans were performed using 64 slice MSCT with contrast and β blocker drugs. Pretest probability was not specified. Invasive angiography was the reference test. Mean age was 62 years. Men comprised 80% of the study population. Mean heart rate was 68 beats per minute.

The authors reported segment based sensitivity, specificity, positive predictive value and negative predictive value for CT as follows: 91.2%, 99.2%, 95.3% and 98.3%, respectively. Of the 1326 segments, 26 (2%) were not assessable. Per patient analysis was not reported. They concluded "that despite a persistent inverse correlation of image quality to patient heart rate or heart rate variability, in 64-slice CT, there is no translation of such effect into deterioration of accuracy." Health outcomes were not reported. Study population included patients at relatively high probability.

Budoff MJ, Rasouli ML, Shavelle DM, et al. Cardiac CT Angiography (CTA) and Nuclear Myocardial Perfusion Imaging (MPI)—A Comparison in Detecting Significant Coronary Artery Disease. Acad Radiol 2007;14:252–257.

Budoff and colleagues reported the results of a case series of 30 patients "to compare the accuracies of CTA and myocardial perfusion imaging (MPI) for identifying symptomatic patients with hemodynamically significant obstructive coronary artery disease (CAD)." Patients with exertional angina or dyspnea who were scheduled for cardiac catheterization were included. Exclusion criteria included renal insufficiency and allergy to contrast media. Scans were performed using electron beam CT with contrast. Pretest probability was not specified. Invasive angiography was the reference test. Mean age was 54 years. Men comprised 70% of the study population.

The authors reported vessel based sensitivity, specificity, positive predictive value and negative predictive value for CT as follows: 94%, 96%, 92% and 97%, respectively. Number of nonassessable segments was not reported. They noted: "The presence of clinically significant CAD was 70% in our study population. This high prevalence could potentially raise sensitivity at the expense of specificity for all tests. The majority of patients underwent elective coronary angiography for the evaluation of chest pain in the outpatient setting. There was most likely a referral bias toward those with positive nuclear tests, raising the sensitivity and lowering the specificity for this test. Patients with a negative noninvasive test are not routinely referred for coronary angiography, therefore creating a referral bias. The effect of referral bias on sensitivity and specificity has been shown in studies with exercise radionuclide ventriculography and exercise thallium imaging. Caution must be used in applying these results in a higher risk population to overall patients likely to have coronary CTA or MPI, who are a much lower risk group." The authors concluded: "CTA accurately detects obstructive CAD in symptomatic patients and may be more accurate than MPI or CAC assessment. Larger studies in a more diverse population are needed." Health outcomes were not reported. Sample size was small.

Cademartiri F, Maffei E, Palumbo A, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in patients with low-to-intermediate risk. Radiol med 2007;112:969–981.

Cademartiri and colleagues reported the results of a case series of 72 patients "to evaluate the diagnostic accuracy of 64-slice computed tomography coronary angiography (MSCT-CA) for detecting significant stenosis ($\geq$50% lumen reduction) in a population of patients at low to intermediate risk." All patients had either atypical chest pain, exertional angina, positive, doubtful or inconclusive stress tests and were scheduled for invasive angiography. Patients with contraindications to contrast were excluded. Scans were performed using 64 slice MSCT with contrast and β blocker drugs. Pretest probability was not specified. Invasive angiography was the reference test. Mean age was 54 years. Men comprised 53% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value for CT as follows: 100%, 91.8%, 95.2% and 100%, respectively. Image quality was considered good in 98.5% of cases. They concluded that "64-slice CT-CA is a diagnostic modality with high sensitivity and negative predictive value in patients at low to intermediate risk." Health outcomes were not reported. Sample size was small. Although low to intermediate probability patients were targeted, the study population included patients at relatively high probability (patients with a positive stress test).

Hausleiter J, Meyer T, Hadamitzky M, et al. Non-invasive coronary computed tomographic angiography for patients with suspected coronary artery disease: the Coronary Angiography by Computed Tomography with the Use of a Submillimeter resolution (CACTUS) trial. European Heart Journal 2007;28:3034–3041.

Hausleiter and colleagues reported the results of a case series of 243 patients "to assess the clinical usefulness of coronary MSCT angiography for the detection of significant CAD in a patient population with an intermediate pre-test probability for having CAD on an 'intention-to-diagnose'-based analysis." Patients with intermediate probability who were scheduled for invasive angiography were included. Exclusion criteria included previous revascularization, renal insufficiency, contraindications to contrast. Scans were performed using 16 or 64 slice MSCT with contrast and β blocker drugs. Pretest probability was defined as "(i) patients with chest pain, dyspnea or with intermittent arrhythmias in the absence of a positive stress test or with an equivocal stress test for myocardial ischemia and (ii) asymptomatic patients with a positive stress test." Invasive angiography was the reference test. Mean age was 62 years. Men comprised 65% of the study population. About 30% of patients were asymptomatic.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value for CT as follows: 99%, 75%, 74% and 99%, respectively. Of the 2683 segments, 254 (9.5%) were considered inconclusive. They concluded: "In patients with an intermediate pre-test probability for having CAD this large, prospective trial demonstrates that non-invasive coronary CT angiography is a very sensitive method for CAD detection. Furthermore, this method allows ruling out CAD very reliably and safely. Finally, 64-slice CT appears to be superior for CAD detection when compared with 16-slice CT." The authors also noted: "The definition of patient inclusion criteria is crucial for investigating new diagnostic techniques. Previous definitions of 'intermediate CAD risk' are mainly based on age, gender, and quality of chest pain. Although some of our patients may have been classified as having a low probability for CAD with the use of these previous definitions, addition of myocardial stress test results as additional inclusion factor in the current study may have allowed for a better discrimination of pre-test probabilities for CAD." Health outcomes were not reported. There was no comparison group. A nonstandard definition of pretest probability was used.

Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-Slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007;93:1386–1392.

Meijboom and colleagues reported the results of a case series of 104 patients "to study the diagnostic performance of 64-slice CTCA in patients with non-ST elevation ACS." Patients with unstable angina or non ST segment elevation myocardial infarction who were referred for invasive angiography were included. Exclusion criteria included previous revascularization, renal insufficiency, contraindications to contract. Scans were performed using 64 slice CT with contrast and β blocker drugs. Pretest probabilities were either high or low as defined by baseline characteristics, troponin or ECG changes." Invasive angiography was the reference test. Mean age was 59 years. Men comprised 72% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value for CT as follows: 100%, 75%, 96% and 100%, respectively. The number of uninterpretable segments was not reported. They concluded: "The 64-slice CT angiography has a high sensitivity to detect significant coronary stenoses and is reliable to exclude the presence of significant CAD in patients who present with a non-ST elevation ACS. The role of CTCA in these patients, particularly in the low-risk group, needs to be further evaluated." Health outcomes were not reported. There was no comparison group. We believe that this article was reviewed earlier as an online publication.

Meijboom WB, van Mieghem CAG, Mollet NR, et al. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. J Am Coll Cardiol 2007;50:1469–1475.

Meijboom and colleagues reported the results of a case series of 254 patients "to evaluate the diagnostic performance and clinical usefulness of 64-slice CTCA in 254 patients with high, intermediate, or low estimated pretest probability of having significant coronary stenosis." Patients had typical angina, atypical angina or nonanginal chest pain and were referred for invasive angiography. Exclusion criteria included history of percutaneous coronary intervention, coronary artery bypass surgery, impaired renal function and allergy to contrast. Scans were performed using 64 slice CT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability for CAD was estimated using the Duke Clinical Score (Pryor, 1993). Of the 254 patients, 105 were estimated to have a high pretest probability while 83 and 68 patients were intermediate and low, respectively. Mean ages were 63 years, 61 years and 50 years for high, intermediate and low probability respectively. Men comprised 92%, 57% and 41%, respectively.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 98%, 74%, 93% and 89%, respectively, for the high probability group; 100%, 84%, 80% and 100%, respectively, for the intermediate probability group; and 100%, 93%, 75% and 100%, respectively, for the low probability group. Of the 4318 segments, 3647 (84%) were included in the analysis. They concluded: "Computed tomography coronary angiography is useful in symptomatic patients with a low or intermediate estimated pretest probability of having significant CAD, and a negative CT scan reliably rules out the presence of significant CAD. Computed tomography coronary angiography does not provide additional relevant diagnostic information in symptomatic patients with a high estimated pretest probability of CAD." Health outcomes were not reported. Sample sizes were small for lower probability groups.

Meijboom WB, Weustink AC, Pugliese F, et al. Comparison of diagnostic accuracy of 64-slice computed tomography coronary angiography in women versus men with angina pectoris. Am J Cardiol 2007;100:1532–1537.

Meijboom and colleagues reported the results of a case series of 402 patients "to ascertain the diagnostic accuracy of CTCA in women versus men with chest pain to detect or exclude the presence of obstructive CAD." Patients with acute or stable chest pain symptoms who were referred for invasive angiography were included. Exclusion criteria included history of percutaneous coronary intervention or coronary artery bypass surgery, impaired renal function and allergy to contrast. Scans were performed using 64 slice CT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 62 years in women and 58 years in men.

The authors reported results separately for women and men and noted: "The sensitivity and negative predictive value to detect significant CAD was very good, both for women and men (100% vs. 99%, p = NS; 100% vs. 98%, p = NS), whereas diagnostic accuracy (88% vs. 96%; p <0.01), specificity (75% vs. 90%, p <0.05), and positive predictive value (81% vs. 95%, p <0.001) were lower in women." Of the 6834 segments, 5735 (84%) were included in the analysis. Combined results were not reported. They concluded: "In conclusion, CT coronary angiography reliably rules out the presence of obstructive CAD in both men and women. Specificity and positive predictive value of CT coronary angiography were lower in women. The sensitivity to detect stenosis in small coronary branches was lower in women compared with men." Health outcomes were not reported.

Min JK, Shaw LJ, Devereux RB, et al. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007;50:1161–1170.

Min and colleagues reported the results of a retrospective analysis of a 1127 patient registry "to determine whether use of CCTA as the primary noninvasive imaging modality in the evaluation of patients presenting with chest symptoms would offer incremental prognostic value for prediction of all-cause mortality." Patients in the registry were "referred for evaluation by CCTA for a variety of indications, including evaluation of symptoms, signs of cardiac disease (abnormal rest or stress test), or asymptomatic patients with peripheral arterial disease, cerebrovascular disease, or multiple coronary artery disease (CAD) risk factors." Scans were performed using 16 slice MDCT with contrast. Pretest probability was not reported. Mean age was 62 years. Men comprised 63% of the study population. Mean follow-up in the registry was 15 months.

The authors reported "The CCTA predictors of death included proximal left anterior descending artery stenosis and number of vessels with ≥50% and ≥70% stenosis (all p < 0.0001)." They concluded: "In patients with chest pain, CCTA identifies increased risk for all-cause death. Importantly, a negative CCTA portends an extremely low risk for death." Results by indication for CTA were not reported. Asymptomatic patients were included. Number of patients who received invasive angiography was not reported. There was no comparison group. Death was determined using the Social Security index. Of the 39 deaths, follow-up data was available for 10 (26%) with 2 of these 10 receiving revascularization. The analysis was performed retrospectively.

Mühlenbruch G, Seyfarth T, Soo CS, et al. Diagnostic value of 64-slice multi-detector row cardiac CTA in symptomatic patients. Eur Radiol 2007;17:603–609.

Mühlenbruch and colleagues reported the results of a case series of 51 patients "to determine the value of 64-slice cardiac CTA for detection of significant coronary artery disease in a population of symptomatic patients." Patients with symptoms of CAD who were scheduled for invasive angiography were included. Exclusion criteria included history of percutaneous coronary intervention or coronary artery bypass surgery, impaired renal function and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 58 years. Men comprised 76% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 98%, 50%, 94% and 75%, respectively. Of the 765 segments, 39 (5%) were excluded. They concluded: "In this symptomatic patient group a 64-slice-MDCT scanner shows good agreement on a segment-based analysis but only moderate agreement on a patient based analysis. The diagnostic accuracy of 64-slice-MDCT coronary angiography is negatively influenced by the high pre-test probability of this symptomatic patient collective." Health outcomes were not reported. Sample size was small.

Pontone G, Andreini D, Quaglia C, et al. Accuracy of multidetector spiral computed tomography in detecting significant coronary stenosis in patient populations with differing pre-test probabilities of disease. Clinical Radiology 2007;62:978-985.

Pontone and colleagues reported the results of a case series of 120 patients "to test the accuracy of MDCT in detecting a significant coronary stenosis as compared with invasive coronary angiography in populations with low and high pre-test likelihood of CAD." Patients with a history of chest pain who were scheduled for invasive angiography were included. Exclusion criteria included history of coronary revascularization, renal insufficiency and allergy to contrast. Scans were performed using 64 slice CT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was determined "using an estimated predicted probability according to American Heart Association (AHA)/ACC guidelines for the management of chronic stable angina, based on age, sex, and symptoms." Mean age was 62 years. Men comprised 71% of the study population. Of the 120 patients, 69 (59%) were classified as low probability while 47 (41%) were high.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 100%, 86%, 90% and 100%, respectively, for the entire study population; 100%, 88%, 85% and 100%, respectively, for the low probability group; and 100%, 58%, 87% and 100%, respectively, for the high probability group. Of the 1160 vessels, 1067 (92%) were assessed. They concluded: "In conclusion, MDCT enables the reliable detection of significant coronary lesions in a population with a low or high pre-test likelihood of CAD. However, in patient groups with a low prevalence of CAD the very high sensitivity and negative predictive value suggest an important clinical role of MDCT, particularly in cases where the purpose is to exclude CAD, thereby avoiding unnecessary invasive procedures. Conversely, in patients with a high pre-test likelihood of CAD, MDCT shows a lower specificity, despite its excellent negative predictive value, suggesting stress test or conventional coronary angiography as the ideal methods to evaluate patients with typical angina. The focus of future studies should be to determine in what clinical setting CT coronary angiography is of most value for early detection of CAD, and how MDCT can compete with other non-invasive diagnostic tests." Health outcomes were not reported. Sample sizes were small for the 2 subgroups.

Pundziute G, Schuijf JD, Jukema JW, et al. Gender influence on the diagnostic accuracy of 64-slice multislice computed tomography coronary angiography for detection of obstructive coronary artery disease. Heart 2008;94:48-52.

Pundziute and colleagues reported the results of a case series of 103 patients "to compare the diagnostic accuracy of current 64-slice MSCT coronary angiography between men and women using conventional coronary angiography as the reference standard." Patients with known or suspected CAD who were scheduled for invasive angiography were included. Exclusion criteria included arrhythmias and allergy to contrast. Scans were performed using 64 slice MSCT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 60 years. Of the 103 patients, 51 were men and 52 were women.

For men, the authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 100%, 89%, 94% and 100%, respectively. For women, the values were as follows: 95%, 93%, 91% and 96%, respectively. One man and 2 women were excluded from the analysis due to inconclusive MSCT. Of the 1485 segments, 53 (4%) were uninterpretable. They concluded: "The findings confirm the high diagnostic accuracy of 64-slice MSCT coronary angiography in both male and female patients." They also noted: "Only patients scheduled for conventional coronary angiography were included in the study, resulting in high disease prevalence (44% in women and 64% in men). Therefore, the findings of the study need to be validated in a population with lower disease prevalence." Health outcomes were not reported. Sample sizes were small for the 2 subgroups.

Pundziute G, Schuijf JD, Jukema JW, et al. Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007;49:62–70.

Pundziute and colleagues reported the results of a case series of 100 patients "to determine the prognostic value of MSCT in patients with known or suspected CAD." Patients with suspected CAD who were referred for evaluation were included. Exclusion criteria included history of coronary bypass, arrhythmias and allergy to contrast. Scans were performed using 16 or 64 slice CT with contrast and β blocker drugs. The reference test varied. Number of patients who underwent invasive angiography was not reported. It was noted that "pretest likelihood of CAD was high in this population." Of the 104 patients enrolled, 4 were excluded due to uninterpretable scans. Mean age was 59 years. Men comprised 73% of the study population.

The authors reported: "Coronary plaques were detected in 80 (80%) patients. During a mean follow-up of 16 months, 33 events (1 death, 3 myocardial infarctions, 4 stable angina hospitalizations, 25 revascularizations) occurred in 26 patients." Of the 1350 segments, 52 (4%) were excluded. They concluded: "Multislice computed tomography coronary angiography provides independent prognostic information over baseline clinical risk factors in patients with known and suspected CAD. An excellent prognosis was noted in patients with a normal MSCT." They noted: "Studies in larger cohorts (with longer follow-up) are clearly warranted to confirm these initial results." The sample size was small. There was no comparison group. Patients were at high probability for CAD.

Schuijf JD, Pundziute G, Jukema JW, et al. Diagnostic accuracy of 64-slice multislice computed tomography in the noninvasive evaluation of significant coronary artery disease. Am J Cardiol 2006;98:145–148.

Schuijf and colleagues reported the results of a case series of 61 patients to determine the diagnostic accuracy of current 64-slice MSCT in the detection of significant coronary artery disease (CAD), using conventional coronary angiography as the gold standard." Patients who were scheduled for invasive angiography were enrolled. Exclusion criteria included contraindications to MSCT. Scans were performed using 64 slice MSCT with contrast. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 60 years. Men comprised 75% of the study population. Of the 61 patients, 1 was excluded since "the heartrate increased to >90 beats/min during MSCT, rendering the complete data set uninterpretable."

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 94%, 97%, 97% and 93%, respectively. Of the 854 segments, 12 (1.4%) were uninterpretable. They reported: "In conclusion, the present study confirms that 64-slice MSCT enables the accurate and noninvasive evaluation of significant coronary artery stenoses." They further noted: "Although visual evaluation will be sufficient in most segments, more precise assessment of the degree of luminal narrowing will be needed in a considerable number of examinations. However, as shown by Leber et al, the ability to visually quantify the grade of luminal obstruction on MSCT remains limited, even with 64-slice technology. Indeed, also in the present study, the degree of stenosis was incorrectly estimated as either more or <50% diameter narrowing in 2 patients, resulting in false diagnoses, although in fact the presence of lesions was correctly identified. Accordingly, the quantification of MSCT coronary angiography is likely to provide enhanced diagnostic accuracy while improving the reproducibility of the technique, and further investments in the development of such algorithms are needed. Finally, the radiation burden of MSCT remains of concern." Health outcomes were not reported. Sample size was small.

Shabestari AA, Abdi S, Akhlaghpoor S, et al. Diagnostic performance of 64-channel multislice computed tomography in assessment of significant coronary artery disease in symptomatic subjects. Am J Cardiol 2007;99:1656 –1661.

Shabestari and colleagues reported the results of a case series of 143 patients "to determine the diagnostic accuracy of 64-slice MSCT in a wider relatively unselected group of patients, some of whom presented with unstable angina pectoris." Patients with suspected CAD or who were scheduled for bypass surgery were included. Exclusion criteria included previous coronary revascularization, renal insufficiency and allergy to contrast. Scans were performed using 64 slice MSCT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 63 years. Men comprised 72% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 96%, 67%, 91% and 83%, respectively. Of the 143 patients, 5 (3.5%) were excluded from the analysis due to nonassessable segments. They noted: "One of major drawbacks of our study was a patient selection bias resultant from the reality that most of our patients were scheduled for ICA. More prevalent CAD in these patients than in the general population may result in overestimation of the diagnostic accuracy of coronary computed tomographic angiography. Moreover, despite inclusion of patients with unstable angina pectoris symptoms in this investigation, they were not assessed in a distinct setting because of their relatively confined number (26 patients). Thus, additional MSCT evaluation remains to be carried out using a higher sample size. Another issue of concern is the radiation dose of 64-slice MSCT, estimated to be more than that of previous generations of MSCT in the study of Hausleiter et al. Some methods are used to decrease the patient radiation dose, including use of an electrocardiography pulsing (tube current modulation) technique. Nevertheless, because of the likelihood of the requirement to apply different phases of the cardiac cycle for image reconstructions, this method was not used in our patients. The third limitation of our study was semiquantitative estimation of stenosis severity using MSCT. However, one should bear in mind that quantitative measurements may not be able to be done in many segments, for example, Raff et al showed that 17% of lesions could not be quantitatively analyzed in their studied subjects." Health outcomes were not reported.

Watkins MW, Hesse H, Green CE, et al. Detection of coronary artery stenosis using 40-channel computed tomography with multisegment reconstruction. Am J Cardiol 2007;99:175–181.

Watkins and colleagues reported the results of a case series of 85 patients "to determine the feasibility and diagnostic accuracy of coronary angiography using 40-channel multidetector computer tomography with multisegment reconstruction for the detection of obstructive coronary artery disease (CAD)." Patients with known or suspected CAD who were referred for invasive angiography were included. Exclusion criteria included previous coronary revascularization, renal insufficiency and allergy to contrast. Scans were performed using 40 channel MDCT with contrast and β blocker drugs. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 59 years. Men comprised 85% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 98%, 93%, 94% and 93%, respectively. Of the total 1,145 segments, 100 (8.7%) were not assessable. They noted: "In conclusion, coronary angiography using 40-channel multidetector computer tomography with multisegment reconstruction accurately detects coronary segments and patients with obstructive CAD, with a small number of nonevaluable cases." Health outcomes were not reported.

Dual Source CT

Johnson TRC, Nikolaou K, Busch S., et al. Diagnostic accuracy of dual-source computed tomography in the diagnosis of coronary artery disease. Invest Radiol 2007;42: 684–691.

Johnson and colleagues reported the results of a case series of 35 patients to assess the diagnostic accuracy of coronary CTA without heart rate modulation with reference to invasive angiography in a cohort of symptomatic patients with a rather high probability of significant CAD." Symptomatic patients with known or suspected CAD who were referred for invasive angiography were included. Exclusion criteria included previous coronary bypass, renal insufficiency and allergy to contrast. Scans were performed using DSCT with contrast. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 60 years. Men comprised 69% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 100%, 89%, 89% and 100%, respectively. Of the 481 segments, 9 (2%) were not assessable and excluded. They concluded: "The comparison of coronary DSCT with QCA [quantitative coronary angiography] shows a very robust image quality and a high diagnostic accuracy in a patient-based as well as a per-segment analysis. Maximal sensitivity and NPV in the per-patient analysis show the strength of the technique in ruling out significant CAD." They further noted: "The main limitation of this study is that it was conducted in a high-risk patient cohort in which the clinical value of CT is limited. The appropriate indication for coronary CTA is to rule out or to identify significant coronary artery disease in patients with an intermediate pretest likelihood. Thus, the study population does not reflect the patient group that can benefit most from coronary CTA, and the sensitivity may be lower and the specificity higher in patients who are examined to rule out coronary artery disease." Health outcomes were not reported. Sample size was small.

Leber AW, Johnson T, Becker A, et al. Diagnostic accuracy of dual-source multi-slice CT coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. European Heart Journal 2007;28:2354–2360.

Leber and colleagues reported the results of a case series of 90 patients "to evaluate the diagnostic accuracy of a newly introduced dual X-ray source MSCT with high temporal resolution (83 ms) to rule out coronary stenoses in a patient cohort with an intermediate likelihood for coronary disease without using HR [heart rate]-modulating premedication." All patients were referred for invasive angiography. Exclusion criteria included renal insufficiency and allergy to contrast. Scans were performed using DSCT with contrast. Invasive angiography was the reference test. Pretest probability was according to scoring reported by Morise and colleagues (Morise, 1997). Mean age was 58 years. Men comprised 63% of the study population.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 95%, 90%, 74% and 99%, respectively. Of the 1232 segments, 16 (1%) were not analyzed. They concluded: "DSCT is a non-invasive tool that allows to accurately rule out coronary stenoses in patients with an intermediate pretest likelihood for CAD, independent of the HR." Health outcomes were not reported. In a letter to the editor on this study, Klepzig commented: "At present, introducing CT scans after an initial superficial examination of the patient is a paradigm shift without scientific evidence for its benefit, but with the potential of misleading patients, exploding costs and damaging our reputation."

Ropers U, Ropers D, Pflederer T, et al. Influence of heart rate on the diagnostic accuracy of dual-source computed tomography coronary angiography. J Am Coll Cardiol 2007;50:2393–2398.

Ropers and colleagues reported the results of a case series of 100 patients "to assess the influence of heart rate on diagnostic accuracy of DSCT coronary angiography." Patients with suspected coronary artery disease who were referred for invasive angiography were included. Exclusion criteria included history of coronary revascularization and renal insufficiency. Scans were performed using DSCT with contrast. Invasive angiography was the reference test. Pretest probability was not reported. Mean age was 61 years. Men comprised 63% of the study population. Of the 100 patients 56 had heart rates < 65 beats/minute while 44 had $\geq$ 65 beats/minute.

The authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 92%, 97%, 68% and 99%, respectively, for the entire study population; 90%, 98%, 66% and 99%, respectively, for the lower heart rate group; and 94%, 95%, 70% and 99%, respectively, for the higher high rate group. Of the 1394 segments, 1343 (96%) were evaluable. They concluded: "All the same, our data provide further support to previous reports that image quality and diagnostic accuracy of DSCT for the detection of coronary artery stenoses is high in patients with a heart rate above the commonly suggested threshold of 65 beats/min. Most likely, this is secondary to improved temporal resolution of DSCT as compared with previous generations of MDCT. Further studies will have to establish the clinical role for DSCT coronary angiography in various clinical scenarios." Health outcomes were not reported. Sample sizes were small for the 2 subgroups.

Emergency Room

Hoffmann U, Nagurney JT, Moselewski F, et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. Circulation 2006;114:2251-2260.

Hoffmann and colleagues reported the results of a case series of 103 patients "to assess computed tomography (CT) angiographic patterns of CAD—any coronary atherosclerotic plaque and significant stenosis—in patients who were being admitted for chest pain and who had negative initial cardiac biomarkers and a nondiagnostic ECG on presentation." Exclusion criteria included clinical instability, renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Mean age was 54 years. Men comprised 60% of the study population. Of the 106 patients enrolled, 3 (3%) did not successfully complete the scan.

The authors reported: "Among 103 consecutive patients (40% female; mean age, 54±12 years), 14 patients had ACS." Total number of patients who underwent invasive angiography was not reported. The authors noted: "Ultimately, the clinical utility of coronary CTA for triage of chest pain patients will depend on the prevalence of ACS and CAD, the proportion of indeterminate CT exams, the cost of the test, and the number of patients who can complete the protocol or who have relative contraindications to undergoing CTA such as asthma or renal failure. Using coronary CTA in patients at very low risk (including patients who would otherwise being sent home) who have a prevalence of ACS <2% would not be cost-effective. We selected patients in whom the ED physicians had decided to rule out myocardial ischemia in the hospital despite the absence of ischemic evidence on ECG and negative initial biomarkers."

The authors concluded: "CTA patterns are different between patients with and without acute coronary syndromes and provide information incremental to traditional risk factors and clinical risk assessment in predicting risk of ACS among patients presenting with acute chest pain to the ED. The absence of coronary artery plaque or stenosis on noninvasive coronary MDCT angiography has a high NPV for the subsequent diagnosis of ACS. These data lay the foundation for larger observational studies and randomized clinical trials that will determine whether coronary CTA may improve the ability to quickly and accurately triage patients with chest pain and has the potential to substantially reduce hospital admissions." Health outcomes were not reported. There was no comparison group. All patients were admitted to the hospital.

Hoffmann U, Pena AJ, Moselewski F, et al. MDCT in early triage of patients with acute chest pain. AJR 2006;187:1240–1247.

Hoffmann and colleagues reported the results of a case series of 40 patients "to determine the accuracy of the noninvasive detection of significant coronary artery stenosis by MDCT, and to ascertain the feasibility of using the findings for triage decision making in patients with acute chest pain who are awaiting hospital admission despite normal initial cardiac enzymes and normal or nondiagnostic ECG on emergency department presentation." Exclusion criteria included clinical instability, renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Mean age was 57 years. Men comprised 53% of the study population.

The authors reported: "The diagnosis of ACS was made in five patients (12.5%)." They reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 100%, 74%, 38% and 100%, respectively. The reference test was not specified. Total number of patients who underwent invasive angiography was not reported.

They concluded: "In conclusion, this pilot study shows that it is feasible to perform coronary MDCT in acutely ill patients. Moreover, our data suggest that MDCT-based detection of significant coronary stenoses has tremendous potential to decrease the number of unnecessary hospital admissions, without reducing appropriate admissions, in patients with chest pain who have nondiagnostic ECG results and normal cardiac enzymes. Large studies are necessary to confirm these results and to determine whether MDCT is cost-effective in this setting. Furthermore, additional MDCT-based triage criteria such as the presence, composition, and morphology of coronary atherosclerotic plaque need to be investigated." Health outcomes were not reported. There was no comparison group. Sample size was small. All patients were admitted to the hospital.

Hollander JE, Litt HI, Chase M, et al. Computed tomography coronary angiography for rapid disposition of low-risk emergency department patients with chest pain syndromes. Acad Emerg Med 2007;14:112-116.

Hollander and colleagues reported the results of a case series of 54 patients to describe 30 day events for low risk patients. All patients presented with chest pain. Inclusion criteria included Thrombolysis in Myocardial Infarction (TIMI) risk score of 0-2 and negative cardiac markers. Exclusion criteria included renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. The main outcome was a composite of cardiac death and acute myocardial infarction within 30 days. Mean age was 46 years. Men comprised 56% of the study population. Fifty-six percent of patients had TIMI score of 0. Follow up was 30 days by telephone.

The authors reported: "Of the 54 patients evaluated after CT coronary angiography, 46 patients (85%) were immediately released from the ED, and none had cardiovascular complications within 30 days." They concluded: "When used in the clinical setting for the evaluation of ED patients with low-risk chest pain, CT coronary angiography may safely allow rapid discharge of patients with negative studies. Further study to conclusively determine the safety and cost effectiveness of this approach is warranted." The authors noted that 3 of 5 patients who had 50-69% stenoses on CT had further noninvasive testing. TIMI risk score was used for classification of unstable angina. There was no comparison group. Sample size was small. Adverse events were self-reported.

Johnson TRC, Nikolaou K, Wintersperger BJ, et al. ECG-gated 64-MDCT angiography in the differential diagnosis of acute chest pain. AJR 2007;188:76–82.

Johnson and colleagues reported the results of a case series of 55 patients "to evaluate the diagnostic value of an ECG-gated 64-MDCT angiography protocol for simultaneous assessment of the pulmonary arteries, coronary arteries, and aorta within a single breath-hold." Patients with acute chest pain were referred for scans. CT was performed "if ECG findings were absent or inconclusive and if the clinical appearance did not suggest a specific cause, making it difficult to determine which vascular area to examine preferentially." Exclusion criteria included inability to hold breath for $\geq$ 15 seconds, renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast. Mean age was 67 years. Men comprised 64% of the study population.

The authors reported: "The cause of chest pain was correctly identified with MDCT in 37 patients. The diagnoses included pulmonary embolism (n = 10), coronary stenosis (n = 9), and aortic dissection (n = 1). In four patients, additional diagnoses were found with other examinations." For the 20 patients who underwent invasive angiography, the authors reported patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 94%, 77%, 84% and 91%, respectively. The numbers of unassessable segments and scans were not reported. They concluded: "With current techniques, ECG-gated CT angiography of the entire chest has very good image quality. The protocol proved helpful in the differential diagnosis of acute chest pain." Health outcomes were not reported. There was no comparison group. Sample size was small.

Rubinshtein R, Halon DA, Gaspar T, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation 2007;115:1762-1768.

Rubinshtein and colleagues reported the results of a case series of 58 patients to examine "performance characteristics of MDCT for diagnosing or excluding an ACS in patients presenting to the ED with possible ischemic chest pain and examined the relation to clinical outcome during a 15-month follow-up period." Patients with possible ischemic chest pain at intermediate risk according to the ACC/AHA guidelines were included. "Intermediate risk patients had (1) clinical symptoms of definite ischemic origin but without high-risk features (not included in the study because of clear diagnosis) or (2) symptoms of uncertain origin but compatible with possible ACS. This included patients with recent chest discomfort at rest not entirely typical of ischemia and free of pain when initially evaluated and without new ECG changes or elevated biomarkers." Exclusion criteria included atrial fibrillation, renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Mean age was 56 years. Men comprised 64% of the study population.

The authors reported: "Overall, ED MDCT sensitivity for predicting major adverse cardiovascular events (death, myocardial infarction, or revascularization) during hospitalization and follow-up was 92% (12/13), specificity was 76% (34/45), positive predictive value was 52% (12/23), and negative predictive value was 97% (34/35)." They noted "larger studies are required to define more accurately the magnitude of benefit achieved and safety of the approach in terms of long-term patient outcome" and concluded that "64-slice cardiac MDCT is a potentially valuable diagnostic tool in ED patients with chest pain of uncertain origin, providing early direct noninvasive visualization of coronary anatomy." Patients had intermediate risks of adverse outcomes. Total number of patients who underwent invasive angiography was not reported. There was no comparison group. Sample size was small.

Rubinshtein R, Halon DA, Gaspar T, et al. Impact of 64-slice cardiac computed tomographic angiography on clinical decision-making in emergency department patients with chest pain of possible myocardial ischemic origin. Am J Cardiol 2007;100:1522–1526.

Rubinshtein and colleagues reported the results of a case series of 58 patients to examine "the impact of 64-slice MDCT scanning on clinical decision-making and patient disposition in patients presenting to the ED with possible ischemic chest pain." Patients had nondiagnostic chest pain syndromes. Exclusion criteria included renal insufficiency and allergy to contrast. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Mean age was 56 years. Men comprised 64% of the study population.

The authors reported: "After MDCT, the diagnosis of acute coronary syndrome was revised in 18 of 41 patients (44%; 16 normal MDCT/widely patent stents, 2 alternative diagnoses), planned hospitalization canceled in 21 of 47 patients (45%; 13 normal MDCT/patent stent, 8 minor branch vessel disease), and planned early invasive strategy altered in 25 of 58 patients (43%; unnecessary in 20 of 32, advisable in 5 of 26 others). Effect of MDCT on clinical decisions was greater in the 36 patients without known preceding coronary disease. In 32 patients discharged from the ED (11 after initial triage, 21 patients after MDCT), there were no major adverse cardiac events (e.g., death, myocardial infarction, unplanned revascularization) during a 12-month follow-up period." Patients had intermediate risks of adverse outcomes. Total number of patients who underwent invasive angiography was not reported. There was no comparison group. Sample size was small.

Meta Analysis

Abdulla J, Abildstrom SZ, Gotzsche O, et al. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. European Heart Journal 2007;28:3042–3050.

Adbulla and colleagues reported the results of a meta-analysis "to evaluate the diagnostic accuracy of 64-slice multi-detector computed tomography coronary angiography (64-SCTA) compared with the standard reference conventional coronary angiography (CCA)." Studies were eligible "if they included patients with proven or suspected CAD using 64-SCTA compared with CCA as standard reference." Analysis was performed using a random effects model (DerSimonian and Laird). Of the 29 studies that meet inclusion criteria, 27 studies (1740 patients) were included. Of these, 19 studies (1251 patients) evaluated the coronary arteries specifically.

The authors reported pooled patient based sensitivity, specificity, positive predictive value and negative predictive value as follows: 97.5%, 91%, 93.5% and 96.5%, respectively. They concluded: "The high diagnostic accuracy of 64-SCTA validates this non-invasive technique as a potential alternative to CCA in carefully selected populations suspected for coronary stenosis." They further noted: "In summary, the current 64-SCTA technique can therefore not be recommended for examination of patients with high probability of CAD and coronary intervention and neither for screening of asymptomatic patients. Ideally, cardiologists should use a pretest probability of CAD in order to avoid further interventions associated with increased radiation risk. Appropriate selection of patients can be performed by a pretest probability of CAD, assessment of lifetime cancer risk, probability of artefacts induced by motion and arrhythmias, as well as patients' ability to cooperate."

Vanhoenacker PE, Heijenbrok-Kal MH, Van Heste R, et al. Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: Meta-analysis. Radiology 2007;244:419-428.

Vanhoenacker and colleagues reported the results of a meta-analysis "to review the literature about the diagnostic performance of multidetector CT angiography for assessment of symptomatic coronary artery disease, with conventional coronary angiography as the reference standard." Study inclusion criteria were scans using $\geq$4 detectors, clinical suspicion of CAD, invasive angiography as reference, data presented to calculate test performance. Of the 928 studies identified, 54 (1474 patients) were analyzed. A random effects model was used.

The authors reported pooled patient based sensitivity of 99% and specificity of 93% for 64 detector CT. They concluded: "From the results of this meta-analysis, we conclude that, with the newer generations of multidetector CT scanners, the diagnostic performance for the assessment of significant coronary arterial stenoses (>50%-diameter stenosis) has significantly improved (P<.05) and the proportion of nonasessable segments has decreased. How this clinically relevant imaging technology will fit in the diagnostic strategy for patients with known coronary artery disease and those who are suspected of having it remains to be determined."

4. MEDCAC

A meeting of the Medicare Coverage Advisory Committee was held on May 18, 2006 to publicly discuss non-invasive diagnostic imaging compared with coronary artery angiography in the diagnosis of coronary artery disease. Information about the meeting including the technology assessment commissioned by CMS, panel questions and voting results and transcript are available on our website at http://www.cms.hhs.gov/mcd/viewmcac.asp?where=index&mid=34. The technology assessment is reviewed in a previous section of this document.

The panel voted on six questions using a 1 - 5 scale with 1 representing a "very unconfident" vote and 5 representing a "very confident" vote. The scores of the nine voting panel members were recorded and the average was calculated.

The first question asked whether the evidence was sufficient to conclude that CTA is accurate to diagnose obstructive coronary artery lesions. The panel voted on this question for both 16-slice CT and 64-slice CT. The average voting member score was 3.44 and 3.56 respectively. On the 1 to 5 scale, a score of 3 represents a vote of "unsure". The second question asked whether the evidence was sufficient to conclude that CTA could accurately determine the anatomic location of obstructive coronary artery lesions. For the 16-slice technology, the average score of the voting members was 4.0 and for 64-slice the average score was 4.11. On the scale, a score of 4 represents a vote of "somewhat confident". Question three asked whether the evidence was sufficient to conclude that CTA could accurately detect the relevant morphology (size, shape, ulceration, etc.) of obstructive coronary artery lesions. The average voting members score was 3.33 for both the 16-slice and 64-slice technologies.

Regarding the panel's confidence regarding whether CTA can replace coronary catheterization to determine treatment of CAD (question four), the average score for 16-slice was 3.22 and for 64-slice was 3.44. When used in addition to catheterization, question five asked whether CTA provided an incremental benefit. The first part of the question asked about the incremental benefit of CTA when performed before catheterization for 16 and 64-slice. The average panel vote was 2.75 and 3.13 respectively. The second part of the question related to incremental benefit when performed after catheterization. For 16-slice, the average panel vote was 2.56 and for 64-slice was 3.00. A score of 2 on the scale represents a vote of "somewhat unconfident".

In question six, the panel vote was 2.44 (16-slice) and 2.67 (64-slice) as to whether the test characteristics were generalizable to the Medicare beneficiary population. On the second part of question six, the panel voted 2.67 (16 -slice) and 3.00 (64-slice) as to whether the diagnostic or treatment strategies using CTA for CAD would provide a net health benefit to Medicare beneficiaries when compared to invasive imaging.

5. Evidence-based guidelines

Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: A scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114;1761-1791.

In 2006, Budoff and colleagues published a joint society statement based on evidence and opinion on the use of CTA in patients with CAD. The authors reported: "The studies that have evaluated the accuracy of EBCT and MDCT "coronary angiography" for the assessment of coronary artery stenoses have been relatively small (up to 149 individuals). They recruited somewhat selected patients (eg, excluding patients with acute coronary syndromes or atrial fibrillation), and all studies have been validated against invasive coronary angiography as a gold standard. No outcomes-based analyses that made further clinical management dependent on the EBCT or MDCT result have been published. However, all studies have convincingly demonstrated a very high negative predictive value of CT coronary angiography (see Table 8). Thus, a "normal" CT coronary angiogram allows the clinician to rule out the presence of hemodynamically relevant coronary artery stenoses with a high degree of reliability. When considering whether to refer a patient for EBCT or MDCT, clinicians must weigh the relative advantages of other testing methods such as exercise testing or stress imaging. The choice of testing will be determined by both local expertise in a given hospital as well as by the patient's specific clinical history. Functional information demonstrating the physiological significance of coronary lesions is still paramount for decision-making related to revascularization. In a clinical context, the high negative predictive value may be useful for obviating the need for invasive coronary angiography in patients whose symptoms or abnormal stress test results make it necessary to rule out the presence of coronary artery stenoses. Especially if symptoms, age, and gender suggest a low to intermediate probability of hemodynamically relevant stenoses, ruling out hemodynamically relevant stenoses by CT coronary angiography may be clinically useful and may help avoid invasive angiography. CT coronary angiography is reasonable for the assessment of obstructive disease in symptomatic patients (Class IIa, Level of Evidence: B). Use of CT angiography in asymptomatic persons as a screening test for atherosclerosis (noncalcific plaque) is not recommended (Class III, Level of Evidence: C)."

6. Professional Society Position Statements

Hendel RC, Patel MR, Kramer CM, Poon M. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation/American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J Am Coll Cardiol 2006;48:1475–1497.

In 2006, a multispecialty group published appropriateness criteria for CT that were developed using a process that "blends scientific evidence and practice experience by engaging a Technical Panel in a modified Delphi exercise." The group produced an appropriateness score for 39 indications. Specific indications that were considered appropriate (score 7 to 9 out of 9) include:

Detection of CAD: Symptomatic—Acute Chest Pain, Intermediate pre-test probability of CAD, No ECG changes and serial enzymes negative - A(7);
Detection of CAD With Prior Test Results—Evaluation of Chest Pain Syndrome, Uninterpretable or equivocal stress test (exercise, perfusion, or stress echo) - A(8).

Pre-test probability of CAD was determined by "a modification of a literature review recommended by the American College of Cardiology/American Heart Association (ACC/AHA) 2002 Guideline Update for Exercise Testing and ACC/AHA 2002
Guideline Update for Management of Patients with Chronic Stable Angina" (references).

Jacobs JE, Boxt LM, Desjardins B, et al. ACR practice guideline for the performance and interpretation of cardiac computed tomography (CT). J Am Coll Radiol 2006;3:677-685.

In 2006, Jacobs and colleagues reported practice guidelines from the American College of Radiology "to help practitioners provide appropriate radiologic care for patients." Recommendations were presented on indications for cardiac CT, physician qualifications and responsibilities. Cardiac CT is indicated for evaluation of "atherosclerosis," and eleven other indications. As noted by ACR: "Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council." The evidence basis for the guidelines is not reviewed to support the recommendations in this article.

7. Public Comments

A. Initial Public Comment Period

CMS received 127 comments during the initial 30-day public comment period. Comments that were submitted via CMS coverage website may be viewed by using the following link: http://www.cms.hhs.gov/mcd/viewpubliccomments.asp?nca_id=206. The full summary of those comments can be found in our proposed decision memorandum on our coverage website.

B. Public Comment Period on Proposed Decision

CMS received 670 comments during this comment period. Ten (10) commenters agreed with the proposed decision to use Coverage with Evidence Development (CED) for 1) symptomatic patients with chronic stable angina at intermediate risk of CAD; and 2) symptomatic patients with unstable angina at a low risk of short-term death and intermediate risk of CAD. Of the others, 649 commenters were opposed, and the remainder provided no clear direction for coverage. Approximately 200 commenters submitted a standardized form letter.

Comment: Approximately 350 commenters stated that using cardiac CTA saves money and reduces the number of invasive cardiac catheterizations and/or other diagnostic tests.
Response: CMS does not look specifically at cost in evaluating evidence for NCDs. We are very interested in knowing whether patients were spared from other procedures, however, we did not locate published evidence to demonstrate that our population (age $\geq$ 65) did not go on to invasive cardiac catheterization or that the use of other noninvasive diagnostic tests were reduced.

Comment: Approximately 250 commenters stated that local policies established by the local Medicare contractor should remain in place and that Medicare should not move forward with an NCD. Some commenters had a specific recommendation to allow the local policies to remain in place until approved Coverage with Evidence Development studies become available to beneficiaries.
Response: CMS agrees and has decided not to move forward with a national coverage determination. Therefore the local Medicare contractor policies remain effective.

Comment: Approximately 300 commenters believe that patient access to the technology will be adversely impacted if Medicare moves forward with the proposed decision.
Response: CMS has decided not to move forward with a national coverage determination; therefore, beneficiary access to the technology remains unchanged.

Comment: Approximately 100 commenters suggested accreditation or training requirements for cardiac CTA facilities and/or physicians that perform and interpret the tests.
Response: CMS has decided that a national coverage determination is not appropriate at this time and, therefore, CMS will not standardize accreditation or training requirements. In general, we do believe that such standards are important to ensure quality patient care. Some local Medicare contractors address this issue in their Local Coverage Determinations.

Comment: Approximately 100 commenters stated that the proposed policy did not address all indications for cardiac CTA and that some were missing.
Response: The proposed decision purposefully only addressed cardiac CTA for use in coronary artery disease, leaving coverage of other indications at the discretion of local Medicare contractors. However, CMS is not issuing a final national policy and, therefore, no clinical indications for cardiac CTA will be addressed at the national policy level at this time.

Comment: Approximately 100 commenters stated that patient health outcomes are inappropriate measures for diagnostic tests such as cardiac CTA.
Response: While CMS is not moving forward with a national coverage determination, we continue to believe that patient health outcomes are an appropriate measure for cardiac CTA and other diagnostic tests. It is our hope that future studies will evaluate health outcomes so that the health benefit of cardiac CTA to the patient and their balance against the risk of radiation exposure can be demonstrated.

Comment: A few commenters stated that newer CT scanners expose the patient to less radiation.
Response: While we are hopeful that the technology will continue to develop in a manner that reduces radiation exposure, we do not have evidence that supports that radiation exposure is balanced with improved health outcomes.

Comment: Some commenters specifically addressed CED. One commenter asked if a registry can satisfy the CED requirement.
Response: Since CMS will not issue a national coverage determination, CED is no longer germane and, therefore, we do not need to interpret the types of studies that would have satisfied the study requirements.

Comment: Some commenters asked that CMS hold off on making a final decision until additional evidence is available for review.
Response: Clinical evidence is constantly being published for cardiac CTA and many other technologies for which CMS have National Coverage Determinations. It is necessary for policies to capture a technology at one point in time while allowing for future development of evidence.

Professional Society and Organization Comments

CMS received a combined comment from the following six professional societies: American College of Cardiology; American Society of Nuclear Cardiology; American College of Radiology, Society for Cardiovascular Angiography and Interventions; North American Society for Cardiac Imaging; and the Society of Cardiovascular Computed Tomography. In their comments, the societies disagree with Medicare's proposal and recommend keeping coverage at the discretion of the local Medicare contractors through local coverage determinations. CMS also received comments from the American Heart Association in which they recommend changes to the indications regarding defining risk of CAD but support the CED model. Comments were also received from the Cardiology Advocacy Alliance who oppose the proposed decision and from America's Health Insurance Plans who agree with the proposal. The Medical Imaging and Technology Alliance submitted comments in which the organization disagrees with the proposed decision and supports continued Local Coverage Determinations. The following comments were submitted by the professional societies or other organizations and are otherwise not specifically addressed above.

Comment: Should Medicare move forward with a national policy, the commenter does not support CED but support national coverage for the following indications:

1. Symptomatic patients with chronic stable angina or anginal equivalent and an intermediate pre-test probability of CAD;
2. Symptomatic patients with possible acute coronary syndrome (ACS), a low risk of short term death and an intermediate probability of CAD;
3. Assessment for presence and course of coronary artery anomalies;
4. Coronary artery evaluation in individuals in whom prior clinical non-invasive coronary artery test data (e.g., ECG or imaging results) are equivocal or discordant;
5. Assessment of bypass graft location (e.g., internal mammary artery) prior to surgical intervention in patients undergoing repeat sternotomy; and
6. Coronary artery evaluation in patients undergoing non-cardiac surgery.

Response: CMS is not issuing a national coverage determination. Therefore, coverage of the above indications remains at the discretion of the local Medicare contractors. Screening patients for CAD prior undergoing non-cardiac surgery is not a covered benefit.

Comment: The commenter stated that there was evidence not evaluated by CMS.
Response: We reviewed the relevant evidence referenced by all commenters and those are summarized under the Evidence section of this document. In addition a complete list of references is available in Appendix C.

Comment: The commenter recommended coverage of patients who cannot undergo non-invasive stress testing because of disability, illness, or morbid obesity.
Response: Since a national coverage determination will not be issued, coverage of the above indication remains at the discretion of local Medicare contractors.

Comment: The commenter states that the proposed decision inappropriately uses the terms "chronic stable angina", "intermediate risk of CAD" and "unstable angina". They suggest that in addition to "chronic stable angina," "anginal equivalent" should be added. Further, they suggest that the more common scores to estimating risk of CAD are Diamond and Forrester or Duke classifications. Regarding "unstable angina" they suggest replacing that language with "possible acute coronary syndrome" because unstable angina implies that a CAD diagnosis has already been made and it is now considered a subcategory to Acute Coronary Syndromes.
Response: For "chronic stable angina" we believe that anginal equivalent is subsumed as part of the definition of chronic stable angina. We agree with the societies that there are additional methods of assessing patient risk of CAD and therefore we are updating the decision memorandum to reference additional classifications. We maintain that "unstable angina" is the appropriate term for the population we are defining and that the definition we reference in the decision does not infer that the diagnosis of CAD has already been made. However, since CMS is not issuing a national coverage determination, the above definitions will be part of the decision memorandum but will not be part of national policy.

Comment: CMS received recommendations on the questions that CMS proposed should be answered by CED studies. The first question proposed by CMS is, "Does cardiac CTA have the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?" The commenter stated that CMS should create separate questions to better focus on capturing the impact of cardiac CTA on clinical management. The commenter also suggested changes to the third listed question, "Does coronary CTA improve health outcomes for patients with acute chest pain who present in the emergency room or other setting?" They recommend focusing the question to address the impact of cardiac CTA on CAD related medication administration and whether CTA reduces the rates of invasive procedure-related complications.
Response: Since CMS is not issuing a national coverage determination, CED questions will not be part of any decision. We do believe these questions should be the focus of future research.

Comment: A commenter has stated that the evidence does not support the use of cardiac CTA for screening asymptomatic patients for CAD.
Response: We agree that the evidence does not support this indication. Further, Medicare cannot pay for screening uses of CTA.

Comments with Evidence
Of the 670 comments received, 45 included citations to published evidence. In total, 153 references were provided. After assessing the references, we determined that 26 met the original search criteria we used in our review. We focused on studies that reported original data and health outcomes. Abstracts were excluded. References that met our criteria are reviewed in the evidence section of this decision memorandum. The complete list of references provided by commenters is available in Appendix C.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act § 1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." § 1862(a)(1)(A).

There has been rapid advancement of the CTA technology from the initial 4 slice machines to the currently favored 64 slice scanners. Studies have been conducted using all these variants. As noted in various studies, the sensitivity and specificity appear to be higher with 64 slice MSCT. In addition, many have reported that the 64 slice MSCT produces considerably better quality images compared to the others. It also appears that this is a general consensus of the professional community and industry that 64 slice MSCT is the preferred choice for coronary CTA. With demonstrated technological improvements and general consensus, we believe that coronary CTA should be performed with 32 slice or better CT machines. Another technology (dual source CT) has been developed but the number of reports (6 with a total of 406 patients) are small and the machines are not yet widely available.

The primary safety concerns with cardiac CTA are the exposure to considerable amounts of radiation and the use of contrast and β blocker medications. While we have not specifically focused on safety of coronary CTA, cumulative health outcomes are directly affected by the safety of any test and safety therefore influences the reasonable and necessary determination.

For a radiation risk reference point, the FDA stated (available at http://www.fda.gov/cdrh/ct/risks.html and in the Appendix A): "In the field of radiation protection, it is commonly assumed that the risk for adverse health effects from cancer is proportional to the amount of radiation dose absorbed and the amount of dose depends on the type of x-ray examination. A CT examination with an effective dose of 10 millisieverts (abbreviated mSv; 1 mSv = 1 mGy in the case of x rays.) may be associated with an increase in the possibility of fatal cancer of approximately 1 chance in 2000. This increase in the possibility of a fatal cancer from radiation can be compared to the natural incidence of fatal cancer in the U.S. population, about 1 chance in 5. In other words, for any one person the risk of radiation-induced cancer is much smaller than the natural risk of cancer. Nevertheless, this small increase in radiation-associated cancer risk for an individual can become a public health concern if large numbers of the population undergo increased numbers of CT screening procedures of uncertain benefit." For radiation dose, the noted: "The effective doses from diagnostic CT procedures are typically estimated to be in the range of 1 to 10 mSv. This range is not much less than the lowest doses of 5 to 20 mSv received by some of the Japanese survivors of the atomic bombs. These survivors, who are estimated to have experienced doses only slightly larger than those encountered in CT, have demonstrated a small but increased radiation-related excess relative risk for cancer mortality."

The radiation exposure from cardiac CTA has received particular attention in recent publications since it may be much higher.

Paul and Abada (2007) reported: "Radiation dose is becoming a major issue for contrast enhanced cardiac multislice CT (coronary CT angiography), since 64-slice CT shows promising results for coronary artery evaluation. The radiation dose delivered for coronary CT angiography using retrospective gating is necessarily high because only part of the total radiation delivered is used for the reconstruction of the image in the current, commonly practised retrospective mode. The "useful" radiation corresponds to a temporal window of one phase of the cardiac cycle (for example the mid-diastole). This temporal window is determined by the rotation time of the machine; its value is about half the rotation time for amonophasic reconstruction. On average, only 20% of the radiation burden is used to reconstruct one phase of the cardiac cycle. In daily practice, computed tomography dose index (CTDI) for coronary CT angiography may reach or pass 100 mGy, with a dose-length product (DLP) of up to 2,000 (100 mGy×20 cm) if the entire thorax is scanned without application of dose-sparing tools. Thus, the effective dose may be up to about 40 mSv in female patients (corresponding to a DLP of 2,000 mGy·cm), and there are associated breast radiation issues. Cardiac patients may be exposed to various sources of medical radiation (including nuclear studies and conventional angiography), with repeated examinations, making radiation exposure risks certain when cumulated radiation dose exceeds 200 mSv. Due to these high radiation levels, it seems essential to minimise the radiation dose associated with cardiac CT examinations. Radiologists should be increasingly careful about radiation dose levels and should attempt to use dose-saving algorithms whenever possible"

The AHA (Budoff et al., 2006) also noted the risk of radiation exposure: "For CT angiography, the higher radiation doses suggest the need for greater forethought when using these tests, and use of these higher radiation exposure tests in asymptomatic persons for screening purposes is not currently recommended." Einstein and colleagues (2007) reported that their "simulation models suggest that use of 64-slice CTCA is associated with a nonnegligible LAR (lifetime attributable risk) of cancer" and that the risk is "considerably greater for women, younger patients, and for combined cardiac and aortic scans." As with most tests and interventions, risks and adverse events should be considered when deciding to perform the test in question and discussed with each patient prior to undergoing the test.

Direct evidence, modeling and the professional society statement about the radiation dose delivered by cardiac CTA demonstrate risks that are not just hypothetical. The importance of negative predictive value for a test such as coronary CTA is predicated in part on the ability to avoid a riskier more invasive test, coronary angiography. In light of these considerations, any assessment of coronary CTA must take the risks into account and requires evidence of compelling benefits.

This analysis of the evidence focused on the following questions:
a. Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?
b. Is the evidence sufficient to conclude that cardiac CTA reduces the need for invasive coronary angiography?
c. Is the evidence sufficient to conclude that the use of cardiac CTA improves health outcomes for patients with acute chest pain who present in the emergency room or other settings?

a. Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?

To evaluate this question on appropriateness, the test characteristics (sensitivity and specificity) and performance (positive and negative predictive values) of cardiac CTA compared to invasive angiography, need to be considered. In general, sensitivity of a specific test is the proportion (percent) of people with the disease who have a positive test for the disease. Specificity is the proportion of people without the disease who have a negative test. Positive predictive value refers to the proportion of people with positive tests that actually have the disease as confirmed by the gold standard reference test (ability of coronary CTA to diagnose CAD compared to invasive angiography). Negative predictive value refers to the proportion of people with negative tests that actually do not have the disease as confirmed by the gold standard (ability of coronary CTA to rule out CAD compared to invasive angiography). Predictive values are determined by the sensitivity and specificity of the test and the prevalence of the disease.

Numerous studies have evaluated these parameters. Several technology assessments, meta-analyses and reviews have been published on coronary CTA in recent years. The BCBS TEC performed and published 2 technology assessments on coronary CTA (2005, 2006). The first evaluated CTA for evaluation of the coronary arteries, in general, while the latter focused on 32 or higher slice CT and use of coronary CTA in the emergency room. Both assessments found that coronary CTA did not meet TEC criteria. Three meta-analyses (Hamon, Schuijf, Sun) and 2 systematic reviews (Janne d'Othee, Stein) have been published and reported pooled test parameters (Table 1). Of the additional 11 published articles that we reviewed, 8 reported test parameters (Table 2). Since our proposed decision, 16 additional studies that reported test characteristics, 2 meta-analyses and 2 articles on prognostic value were reviewed.

Overall the reported sensitivity, specificity and predictive values are generally above 80-90%. However, these estimates have limitations in applicability and generalizability due to patient selection and potential bias. Although most studies did not report pretest probability, almost all patients enrolled in the reviewed studies were likely at relatively high pretest probability for CAD, since these patients were already on the schedule for invasive coronary angiography (selected patient population). In general, test sensitivity and specificity will be higher when calculated in patients with more severe disease. The sensitivity and specificity estimates for coronary CTA based on high probability patients are not directly applicable to other patients at low or intermediate probability. Comparative estimates calculated from data on low (Meijboom, Pontone) or intermediate (Cademartiri, Hausleiter, Leber) probability patients were reported but were based upon small samples in selected patients for the different subgroups. Hausleiter reported values but used a nonstandard definition of pretest probability. The reported sensitivity was 99-100% and specificity 75-98% in the studies with defined intermediate probability patients scheduled for invasive angiography. Unbiased estimates most likely would be lower given the reduced severity of disease (spectrum bias[1]). These estimates, particularly for intermediate probability patients, are arguably more important since the role of coronary CTA appears to be more supported in these patients to avoid invasive angiography. The decision for invasive angiography is clinically variable for these patients; whereas, in high probability patients, invasive testing and interventions are likely to be recommended. Bias may also have been introduced if the interpretation of the CTA images were influenced by the results of the invasive angiography or other clinical data at the time of reading (unblinded). These issues are reflected in a 1999 report on design related bias in studies of diagnostic tests by Lijmer and colleagues, who noted: "The optimal design for assessing the accuracy of a diagnostic test is considered to be a prospective blind comparison of the test and the reference test in a consecutive series of patients from a relevant clinical population. A relevant clinical population is a group of patients covering the spectrum of disease that is likely to be encountered in the current for future use of the test."

The reported sensitivities and specificities also appear to vary somewhat, according to number of slices with a general trend that suggested the 64 slice machines had the best test estimates. This is consistent with the general consensus that 64 slice MSCT produces better images than the other variants.

Similar to sensitivity and specificity, the reported positive and negative predictive values of coronary CTA based on high probability patients are not directly applicable to low or intermediate probability patients because the prevalence of disease is different. The predictive values would very likely be lower if calculated using data from low or intermediate probability patients since these subpopulations have lower prevalence of CAD. If sensitivity and specificity were also to fall based on probability, then the reduction in predictive values would be more precipitous. The positive and negative predictive values for low probability populations ranged from 75-95% and 100% and for intermediate probability populations 74-95% and 80-100%, respectively. However, these studies enrolled patients who were scheduled for invasive angiography and may potentially have selection and referral biases. As noted by several authors (Budoff, Hamon, Johnson), test parameters may vary according to patient selection and disease prevalence. Thus, these studies on intermediate probability patients scheduled for invasive angiography do not represent the most clinically relevant population of patients likely to undergo cardiac CTA. The estimates from higher probability populations are not generalizable, therefore the test characteristics and performance for the representative populations have not been adequately determined. The test characteristics of cardiac CTA in a true, unselected intermediate probability population remain understudied. The ability of coronary CTA to diagnose or exclude CAD for the majority of patients is unclear with the current evidence base.

Also problematic is the percentage of uninterpretable segments or uninterruptible images that have been reported (range from 4-29%), since these patients would likely then undergo invasive angiography. In a systematic review, Stein and colleagues (1996) reported: "One limitation has consistently been that a substantial number of coronary artery segments could not be evaluated for stenosis because of insufficient image quality."

In addition, the two studies that reported prognostic value did not have comparison groups. The lack of comparison groups limits inferences about the incremental benefit of adding cardiac or coronary CTA, if any, to current well accepted approaches. It is also unclear how the results of CTA influenced, if at all, subsequent treatments and interventions in these studies. An important role of a prognostic test would be to help modify treatment and outcome appropriately; however, this has not been demonstrated. In the study by Min and colleagues (2007), the data were incomplete since "follow-up was available in 10 of 39 individuals who died" and the analysis was performed retrospectively. In general, predictive models need to be independently validated. In the study by Pundziute and colleagues (2007), the results of CTA did not appear to be used in the decision for subsequent revascularization, as the authors noted: "The decision for revascularization was based on worsening angina and/or the presence of ischemia on noninvasive testing." They also noted: "Studies in larger cohorts (with longer follow-up) are clearly warranted to confirm these initial results."

The AHA scientific statement noted that the reported high negative predictive values of coronary CTA may be "clinically useful" especially for patients with "low or intermediate probability of hemodynamically relevant stenoses" (Budoff et al., 2006). However, this statement appears to be based more on clinical opinion than evidence from research studies. As noted above, robust estimates of NPV have not been reported for these patients. This is reflected in the AHA classification given to coronary CTA for suspected CAD [Class IIa (conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/ efficacy of a procedure or treatment: weight of evidence/opinion is in favor of usefulness/efficacy.), Level of Evidence: B).[2]

We do not believe the evidence we have reviewed demonstrates that cardiac CTA has the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography. Some preliminary evidence from case series on relatively high probability patients have been reported but not for the patients of most interest, the ones with intermediate probability of CAD. Additional research to determine test characteristics and performance is needed for these patients.

b. Is the evidence sufficient to conclude that cardiac CTA reduces the need for invasive coronary angiography?

One of the suggested benefits of cardiac CTA is the reduction or avoidance of invasive angiography. However, none of the studies that evaluated diagnostic test performance were designed to generate evidence on reduction or avoidance of invasive angiography, since almost all patients were at relatively high probability and were already scheduled to undergo invasive coronary angiography. These studies also did not follow-up on health outcomes. One randomized trial (Goldstein et al., 2007) provided information on patients determined to be at low risk for myocardial infarction and complications that received CTA compared to standard of care. At 6 months, there was no significant difference in the number of cumulative cardiac catheterizations (12% in the MSCT group compared to 7% in standard care; p-value=0.24). The pretest probability of CAD was not specifically reported but this study questions the need for CTA in these low risk patients since outcomes were not influenced by the use of CTA. No study has been published on patients with pretest determination, imaging and follow-up. There is insufficient evidence to conclude under 1862(a)(1)(A) that cardiac CTA reduces the need for invasive angiography.

The AHA scientific statement noted a similar finding: "No outcomes-based analyses that made further clinical management dependent on the EBCT or MDCT result have been published" (Budoff et al., 2006). Under certain circumstances, MDCT may actually lead to increased non-invasive and invasive testing, if image quality is poor. Gershlich and colleagues from the British Cardiovascular Society (2006) reported: "Inappropriate use of MDCT as a first-line investigation at its current state of development is likely to result in an unwanted expansion in the need for non-invasive functional tests and even CA" (coronary angiography).

The ACC/AHA guidelines (2002) noted: "Patients with a low-risk exercise test result (e.g., those with a predicted average annual cardiac mortality rate less than or equal to 1% per year) can be treated medically without need for referral to cardiac catheterization. Patients with a high risk exercise test result (e.g., patients with a strongly positive test result in Fig. 2 [Appendix A] or predicted average annual cardiac mortality rate greater than or equal to 4% per year) should usually be referred for cardiac catheterization. Patients with an intermediate-risk exercise test result (e.g., predicted average annual cardiac mortality rate of 2% to 3% per year) should be referred for additional testing, either cardiac catheterization or an exercise imaging study. An intermediate-risk stress test result in a patient with evidence of left ventricular dysfunction should usually prompt referral for cardiac catheterization."

c. Is the evidence sufficient to conclude that the use of cardiac CTA improves health outcomes for patients with acute chest pain who present in the emergency room or other settings?

In the 2006 assessment, the BCBS TEC reviewed 2 studies (White et al., 2005; Sato et al., 2005) on the use of cardiac CTA for patients with chest pain in the emergency room. They stated that "these data do not demonstrate that CTA is an effective test for diagnosis of chest pain in the ER" (BCBS TEC, 2006). Although the settings were emergency rooms, neither study was designed to evaluate health outcomes. No follow-up of health outcomes were reported.

We reviewed eight additional studies: one randomized trial of 197 low risk patients (Goldstein et al., 2007) and six reports of five case series of 341 patients. As noted above, the trial by Goldstein and colleagues evaluated low risk patients who presented to the emergency room with chest pain using 64 slice MSCT. They reported no deaths or myocardial infarctions in either group at 6 months. There were no significant differences in rate of cumulative catheterizations, cumulative angioplasty and bypass surgery at six months. In the case series reported by Olivetti, there was no comparison group and health outcomes were not presented. The study of short-term health outcomes reported on intermediate risk patients by Hollander was small and did not have a comparison group. Two studies (Hoffman, Hoffman) were conducted on patients that were admitted to the hospital. One study (Johnson) described general uses of CTA and did not report health outcomes. Two studies (Hollander, Rubinshtein) presented evidence that CTA was considered in the clinical decision making of patients that presented with acute chest pain. These studies also did not include a comparison group. Without comparison groups, it is difficult to determine the added value of CTA and how the results of CTA influenced treatments and outcomes, as noted above. In the Hollander study, two patients with normal cardiac CTA scans were still admitted to the hospital. This is concerning since it does not support the clinical utility of a normal scan as suggested by proponents.

For low risk patients, the randomized trial by Goldstein did not support the use of cardiac CTA. We believe that the results from this trial provide preliminary evidence against the use of cardiac CTA; however, we also recognize the importance of substantiating these findings in other studies at different centers. The study by Hollander suggested the majority of low risk patients could be discharged without 30 day cardiovascular complications. As recommended in the ACC/AHA guidelines, exercise stress testing was used for subsequent evaluation. For the majority of patients in this setting, the recommended protocol includes exercise testing. To confirm or refute the initial evidence on the role of CTA for the majority of low risk patients in the emergency room setting, additional trials comparing cardiac CTA to the current recommended standard of care (likely to include exercise testing) are needed.

Although the studies by Hollander and Rubinshtein were small (112 total patients) and did not have comparison groups, they provided preliminary evidence of the potential role of CTA. As noted earlier, health outcomes are more important than test characteristics, even for diagnostic tests. The value of a diagnostic test is in how the test results alter treatment and subsequently health outcomes. If the results of a test do not directly affect patient management, then it is unlikely to influence outcomes.

As noted by Rubinshtein and colleagues, "larger multicenter studies are needed to better define the true accuracy and incremental benefit achieved." This position is consisted with our decision for coverage with evidence development. These studies highlight the promising but still under-studied benefits (and risks) in the emergency room setting.

The uncertainty of how coronary CTA fits into the currently recommended clinical pathways (AHA/ACC and ACP guidelines) was reflected in the AHA scientific statements as follows: "When considering whether to refer a patient for EBCT or MDCT, clinicians must weigh the relative advantages of other testing methods such as exercise testing or stress imaging. The choice of testing will be determined by both local expertise in a given hospital as well as by the patient's specific clinical history. Functional information demonstrating the physiological significance of coronary lesions is still paramount for decision-making related to revascularization."

Screening for CAD with Coronary CTA in Asymptomatic Individuals

From an epidemiologic standpoint, screening refers to the identification or detection of unrecognized, asymptomatic disease. Screening is important for conditions that cause significant morbidity and mortality when appropriate tests and treatments that improve health outcomes when provided at an earlier stage in the course of the disease are available. The use of coronary CTA for CAD screening has been suggested for asymptomatic (without chest pain syndrome) individuals. However, no randomized trials have been conducted and published on this use of CTA. No health outcomes have been studied for these patients. The criteria for an appropriate screening test have not been met. A number of technology assessments have been negative (BCBS TEC, HTA TEC). The AHA guidelines (Budoff et al., 2006) for coronary artery calcified plaque noted: "It is not recommended to use CACP measure in asymptomatic persons to establish the presence of obstructive disease for subsequent revascularization (Class III, Level of Evidence: C)." The ACC/AHA ranked detection of CAD with CTA as inappropriate for low and moderate risk patients and uncertain for high risk patients (Hendel, 2006). Thus screening for CAD with coronary CTA is not recommended in asymptomatic individuals.

Congress has not established a screening benefit for cardiac CTA for the diagnosis of CAD; thus, the use of cardiac CTA to screen asymptomatic patients for CAD is noncovered.

Future Research

We believe that large, well designed, prospective studies that enroll relatively unselected patients from community practice with intermediate pretest probabilities are needed to answer the three questions above regarding the ability of cardiac CTA to diagnose or exclude CAD, whether it can replace invasive angiography; and whether it improves health outcomes for patients with acute chest pain who present in the emergency room or other settings. Studies targeting clinically relevant populations are important since diagnostic characteristics most likely will vary with severity and prevalence. A comparison to a reference test is also required to calculate test parameters. The choice of a reference test would depend in part on how cardiac CTA fits into current practice guidelines. A comparison group is also needed to determine the incremental benefit of adding CTA for prognosis.

To specifically answer the question of whether cardiac CTA can replace invasive coronary angiography, we believe large, well designed, prospective studies with pre-specified health outcomes and comparison groups in the clinically relevant populations are needed. Comparison groups are important since traditional methods for risk assessment, and thus need for angiography and catheterization, exist and have been more fully tested. For example, exercise testing is a well accepted standard.

The AHRQ technology assessment performed by the Duke EPC provided some additional recommendations for future research, quoted as follows:

There are three primary types of evidence that could address the question of substitution of non-invasive for invasive imaging: a randomized trial, an observational study ("natural experiment"), or a decision model.

A randomized trial could take several forms and could use either surrogate or patient-related outcomes. For example, patients with suspected CAD could be randomized to a strategy of "usual diagnostic evaluation," including invasive angiography when indicated, or usual diagnostic evaluation plus option for non-invasive coronary imaging. Alternatively, the patients could be randomized between early invasive and early non-invasive coronary imaging. Outcomes could include hard events such as death or MI, as well as efficiency measures including resource consumption and costs.

A "natural experiment" observational study would examine apparently similar patients referred for alternative diagnostic strategies, including early invasive, early non-invasive coronary imaging, and stress imaging. The notion of a "natural experiment" assumes that there is an element of randomness in clinical practice that can be exploited analytically. If the use of a technology in the practice community has matured to the point where there is significant confounding with patient characteristics, even advanced statistical adjustment techniques may not suffice to uncover unconfounded outcomes.

A decision model would examine the most likely diagnostic strategies of interest along with predicted health outcomes and resource use. Since there is a high level of dependency of test performance and treatment benefit and harm on clinical context, such considerations would likely require separate models. Further, sensitivity analyses to identify effects on decision thresholds are a central part of such an exercise.

Conclusions

In summary, there is uncertainty regarding any potential health benefits or patient management alterations from including coronary CTA in the diagnostic workup of patients who may have CAD. No adequately powered study has established that improved health outcomes can be causally attributed to coronary CTA for any well-defined clinical indication, and the body of evidence is of overall limited quality and limited applicability to Medicare patients with typical comorbidities in community practice. The primary safety concerns with cardiac CTA are the exposure to radiation and the use of contrast and β blocker medications. However, while public comments and specialty society opinions following the CMS proposed decision to use CED did not dispel the uncertainty of the test's clinical utility, they did strongly favor maintaining the local coverage policies for CTA. In light of this, CMS has decided to make no change in the current NCD.

CMS wishes to foster the necessary health outcomes research and establish evidence-based diagnostic strategies by encouraging affected Medicare patients to enroll in rigorously designed studies. Absent any reported additional serious patient harms, further national coverage reconsideration of coronary CTA will depend upon peer-reviewed publication and critical evaluation of convincing new evidence.

Additionally, we believe that current guidelines are inadequate to provide appropriate guidance to patients and providers as to the appropriate inclusion of CTA into the diagnostic milieu in the workup of chest pain. We are concerned that providers are using CTA as an additional test added to exercise testing and nuclear imaging rather than thoughtfully considering the appropriate mix of these tests. We encourage the specialty societies to quickly develop this type of guidance.

IX. Summary

The Centers for Medicare and Medicaid Services (CMS) has decided to make no change to section 220.1 of the National Coverage Determination Manual titled "Computed Tomography" (Pub. 100-3, 220.1). We have decided that no national coverage determination on the use of cardiac computed tomography angiography for coronary artery disease is appropriate at this time and that coverage should be determined by local contractors through the local coverage determination process or case-by-case adjudication.

Appendix A - Diagrams and Tables [PDF, 427KB]

APPENDIX B

General Methodological Principles of Study Design
(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.

- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix C – Citations provided through public comments

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[1] Ransohoff and Feinstein noted: "Unless an appropriately broad spectrum is chosen for the diseased and nondiseased patients who comprise the study population, the diagnostic test may receive falsely high values for its "rule-in" and "rule-out" performances."

[2] Reproduced from Budoff et al., 2006:
Classification of Recommendations

- Class I: Conditions for which there is evidence, general agreement, or both that a given procedure or treatment is useful and effective.
- Class II: Conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/ efficacy of a procedure or treatment.
    - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
    - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Conditions for which there is evidence, general agreement, or both that the procedure/treatment is not useful/ effective and in some cases may be harmful.

Level of Evidence

- Level of Evidence A: Data derived from multiple randomized clinical trials
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies
- Level of Evidence C: Consensus opinion of experts

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